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THE CHEMOTHERAPY AND SERUM THERAPY OF PNEUMOCOCCUS AND STREPTOCOCCUS MENINGITIS

I. A RÉSUMÉ OF THE PRESENT STATUS OF THE TREATMENT OF SEPTIC MENINGITIS, WITH THE RECOMMENDATION OF A METHOD *

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I believe it may be stated without fear of contradiction that the most dreaded complications of infections of the ear, mastoid and nasal accessory sinuses, are acute suppurative pneumococcus, streptococcus and staphylococcus meningitis. This is true because of the extremely high mortality with ordinary and present-day methods of treatment, consisting of spinal punctures and the intraspinal injection of immune serums. During the past seven years, I have seen four cases of acute purulent streptococcus and forty-one of pneumococcus meningitis of otitic or nasal origin, or following fractures of the base of skull, in all of which the patients died. It may be that streptococcus meningitis occasionally develops without a primary focus of infection in the upper respiratory tract, or without a preceding fracture of the skull opening up a pathway for infection of the meninges, but I have not seen any cases of this kind. It is true, however, that pneumococcus meningitis may develop without discoverable primary foci in the upper respiratory tract, especially during the course of pneumonia, but in my experience these have been most frequently instances of acute meningeal congestion, better known as "serous meningitis" or "meningismus," with an increased amount of cerebrospinal fluid free of pus cells and organisms. Occasionally, however, a clear fluid of this kind may show pneumococci in culture, but the prognosis of pneumococcus meningitis of other than otitic or nasal origin is always better than those conditions which develop from sinus thrombosis and thrombophlebitis, the labyrinth, etc.

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The frequency of septic meningitis of otitic and nasal origin is difficult to estimate. It is not uncommon for signs of meningeal irritation to develop in the course of extensive infection of the labyrinth, mastoid cells and lateral sinus with phlebitis and thrombosis, but these usually disappear on the establishment of surgical drainage of these foci when they are due to direct extension with the production of a localized but aseptic meningitis, and are not included in the present discussion. Yerger [1] has stated that sixty-three cases of septic meningitis developed among 1,254 patients with otitis media treated during a period of nine years in the Cook County Hospital, and estimates that about 5 per cent of those with otitic and 1 per cent of those with nasal accessory sinus infections may develop meningitis. Cultures were made of twenty-five of these cases; streptococci were found in 57 per cent and pneumococci in 43 per cent. My experience has been that in the majority, the infections are pneumococcic. Neal [2] states that after meningococcus meningitis, infections with pneumococci and streptococci rank next in frequency, followed by occasional instances of *B. influenza* infections and rarely by staphylococcus and *B. coli* meningitis. Netter and Césari [3] have recently reported that of sixty cases of pneumococcus meningitis observed by them, only six patients recovered, and the mortality has been estimated in the neighborhood of 93 per cent. But I am quite sure that the mortality of acute, diffuse purulent streptococcus and pneumococcus leptomeningitis of otitic or nasal origin is higher, and more closely approaches 100 per cent when treated by the usual method of spinal puncture and intraspinal injection of antistreptococcus or antipneumococcus serum. It is realized that some successes have been recorded in the literature, but so far this has not been my good fortune, although I have seen life apparently prolonged by this plan in four cases of pneumococcus meningitis. In passing, I may also mention having seen two patients with alleged pneumococcus meningitis recover. My bacteriologic examinations of the spinal fluids in both of these showed them to be meningococcus, rather than pneumococcus, infections, which suggests the possibility of some reported recoveries being really cases of mistaken diagnoses.

It is not my purpose to discuss the mechanism of infection in septic meningitis, or the question of diagnosis which at times present many difficulties, but to draw attention to this frequency of septic meningitis, the very high mortality, the necessity for investigation toward evolving more efficient means for treatment, and to summarize briefly the results observed

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1. Yerger, C. F.: Meningitis of Otitic Origin, J. A. M. A. **79**:1924 (Dec. 2) 1922.

2. Neal, J. B.: Meningitis, J. A. M. A. **82**:1429 (May 3) 1924.

3. Netter, A., and Césari, E.: Bull. et mém. soc. méd. d. hôp de Paris **47**:763 (May 25) 1923. Hallé, J.: Ibid., p. 757.

in the chemotherapy and serum therapy of pneumococcus and streptococcus meningitis, with special reference to the treatment of experimentally produced septic meningitis by these agents and by simple lavage of the subarachnoid space. The details of these experiments, conducted with the assistance of Miss Anna M. Rule and Mr. Bernard Madden, are given in the succeeding pages.

PRODUCTION OF EXPERIMENTAL MENINGITIS

In our experiments, we have employed highly virulent cultures of a type I pneumococcus and a hemolytic streptococcus. Rabbits were first employed because it is so easy to produce severe and rapidly fatal meningitis in them, especially by intracisternal injections of the organisms, but we finally abandoned them because of the frequency with which fatal bacteremias developed. White rats and guinea-pigs were next employed because of their higher natural immunity to both pneumococci and streptococci, but they proved too small for satisfactory therapeutic experiments, although suppurative meningitis was successfully produced by intracisternal injections of the cultures or by trephining with subdural injections. We have, however, employed a very large number of rats for determining the effects of subthecal injections of the medicaments alone, but finally abandoned them for dogs, because lavage and drainage could not be successfully practiced in such small animals.

Most of our experiments, therefore, have been conducted with dogs of 5 to 10 Kg. in weight. They have proved very valuable because of the readiness and ease with which severe suppurative meningitis could be produced by intracisternal injections. As a general rule, we introduced under ether anesthesia 0.1 cc. of an approximately 1 : 5 dilution of twenty-four hour brain-hormone broth culture of hemolytic streptococcus of extremely high virulence per kilogram of weight, or 0.1 cc. of a 1 : 50 to 1 : 100 dilution of a similar culture of pneumococcus per kilogram. Generally, symptoms of meningitis were apparent within twenty-four hours after infection with pneumococci, but were sometimes delayed up to four days in the case of streptococci. Treatment was generally delayed until symptoms appeared, and these signs and symptoms, including leukocytosis, were typical of acute fulminating septic meningitis and similar to those observed in human beings. The cerebrospinal fluids were always cloudy and purulent, containing hundreds or thousands of pus cells per cubic millimeter, as well as large amounts of protein and myriads of organisms. Untreated controls, which were included in every experiment, usually died within five days after the onset of symptoms, and at necropsy showed the typical gross and histologic changes of acute suppurative leptomeningitis with pus distributed throughout the lateral ventricles and in both the cerebral and spinal subarachnoid spaces. During observation, the dogs were kept

under the influence of morphine and provided with special care. All treatments were given under ether anesthesia. Occasionally the amounts of culture injected were too small to produce fatal meningitis of the controls, but under these conditions the results were excluded. Bacteremias with positive cultures of the heart blood sometimes occurred, but probably not much more frequently than positive blood cultures are encountered in human beings with severe septic meningitis. As a general rule, the experimental infections were more severe and fulminating than septic meningitis of human beings, and we feel assured that any method of treatment proving efficacious in their treatment would hold much promise of success in the treatment of meningitis of human beings, provided it was instituted sufficiently early in the disease.

THE CHEMOTHERAPY OF SEPTIC MENINGITIS

Following the investigation by Idzumi and me [4] on the treatment of experimental pneumococcus meningitis of rabbits with intraspinal injections of ethylhydrocuprein alone, or in combination with homologous serum, I thought that an improved method of treatment was at hand, but not one of eleven patients whom I have treated by these means made a recovery, although the lives of three were prolonged so greatly over the usual time that hopes for complete success were entertained. It is true that Idzumi and I were able to influence the mortality of pneumococcus meningitis of rabbits only slightly, and only when treatment was begun within a few hours after infection and before the onset of symptoms, which were favorable conditions obviously impossible of duplication in practice. In the present series of experiments, no better results were observed in the treatment of experimental pneumococcus meningitis of dogs treated with intravenous, intracisternal and intraventricular injections of the compound, although somewhat more encouraging results were secured by combination with the administration of pneumococcus antibody solution, and especially with lavage of the ventricles to the cisterna magna with simple saline solution.

The dose of ethylhydrocuprein hydrochloride by repeated intracisternal or intraventricular injection cannot with safety be much more than 0.0002 to 0.0003 Gm. per kilogram of body weight, and corresponding to 12 to 18 cc. of a 1:1,000 solution for an adult of average weight, although by intraspinal injection somewhat larger amounts may be administered after removal of an equal or larger volume of spinal fluid. We have confirmed again its high bactericidal value for the pneumococcus in purulent spinal fluids, but I am convinced that almost nothing is to be expected in the way of recovery of patients with diffuse

4. Idzumi, G., and Kolmer, J. A.: J. Infect. Dis. **26**:355 (April) 1920.

pneumococcus leptomeningitis treated with this compound alone by intraspinal, intracisternal, intraventricular or intravenous administration.

As mercurochrome-220 soluble was used so widely and with some success during the past few years in the treatment of bacterial infections, it was but natural to give it a trial in the treatment of septic meningitis. I have had no clinical experience with it in such cases, but Young, Hill and Scott [5] have recently summarized six cases, with varying results. Three of these are from the practice of Dr. A. H. Schwartz of Duluth, Minn.: two "of brain and meningeal infection, which were the result of mastoids," and the third of brain abscess. The first two patients recovered following the administration of this compound, and the third died. The other three cases, all of meningitis, were from the practices of G. T. Tyler, Greenville, S. C., Dr. B. Berghausen, Cincinnati, and Dr. D. S. Adams,[6] Worcester, Mass. All three of these patients succumbed.

In our experiments the repeated intravenous injection of mercurochrome in doses of 0.005 to 0.008 Gm. per kilogram had no appreciable effect on the course or mortality of experimental pneumococcus and streptococcus meningitis of dogs. We also observed that the dose by intracisternal or intraventricular injection should not be much more than 0.0001 to 0.0003 Gm. per kilogram, corresponding to 1 to 3 cc. of a 1:1,000 solution, but treatment by these routes of administration also failed to influence appreciably the infections, and it is our opinion that, while mercurochrome may aid in removing the bacteremia (septicemia) sometimes developing in meningitis, nothing is to be expected in the way of a direct effect on the infected meninges, although it has proved of some value by intravenous injection in the treatment of severe mastoid infections.

Considerable interest is also aroused by the possibilities of gentian violet, neutral acriflavine and rivanol [7] in the treatment of streptococcus and pneumococcus meningitis, since these dyes are known to exert a high and selective bactericidal activity for gram-positive organisms. Royster [8] has reported one case of streptococcus meningitis treated with about 16 intraspinal injections of small amounts of gentian violet, and with prolongation of life ascribed to the influence of the dye, but I know of no other recorded cases treated in this manner, and have had no clinical experience myself with the dyes in the treatment of septic meningitis.

5. Young, H. H.; Hill, J. H., and Scott, W. W.: Treatment of Infections and Infectious Diseases with Mercurochrome-220 Soluble, Arch. Surg. **10**:813 (May) 1925.

6. Adams, D. S.: Boston M. & S. J. **191**:781 (Nov. 20) 1924.

7. Rivanol has been under consideration for some time by the Council on Pharmacy and Chemistry, but the claims made for it have not been substantiated by suitable evidence.

8. Royster, L. T.: Report of a Case of Streptococcic Meningitis Treated with Injections of Gentian Violet, Am. J. Dis. Child. **28**:34 (July) 1924.

We have found these three dyes capable of destroying pneumococci and streptococci in vitro in purulent spinal fluids, but the tolerated dose by intracisternal or intraventricular injection in the treatment of infected dogs usually was not more than 0.0001 to 0.0004 Gm. per kilogram, corresponding to 6 to 24 cc. of 1:1,000 solutions for adults weighing about 130 pounds (59 Kg.).

Unfortunately, however, the repeated subthecal administration of these amounts were without appreciable influence on the course and mortality of the disease in dogs; intravenous injections of 0.005 to 0.008 Gm. per kilogram were likewise ineffective, although we sometimes found that the injected and stained ventricle contained less pus or none at all when pus was otherwise widely distributed. This result was observed with all three of the dyes, and may be interpreted as evidence indicating some degree of local bactericidal effect, but no constant influence was exerted on the duration of life or mortality.

We feel, therefore, that the treatment of streptococcus and pneumococcus meningitis of human beings by spinal puncture and the intraspinal, intracisternal or intraventricular injection of these dyes is not to be expected to yield a successfuul result, although their intravenous injection may prove of aid in overcoming an infection of the blood if bacteremia is found to be present.

Chemotherapy alone, therefore, has little or nothing of real value to offer today in the treatment of severe septic meningitis, if treatment consists of the usual method of draining the purulent cerebrospinal fluid and injecting ethylhydrocuprein, mercurochrome, gentian violet, neutral acriflavine or rivanol subthecally or intravenously. It does not appear possible to introduce sufficient by subthecal injection to influence materially the infections, and it is doubtful if intravenous injections are capable of actually effecting the destruction of organisms in the infected meninges and cerebrospinal fluid. But if means are provided for draining away the purulent cerebrospinal fluid, and especially for lavage of the ventricles and subarachnoid space in general, we believe that the administration of these agents, and particularly of ethylhydrocuprein and the dyes, may be useful as adjuvant measures.

THE SERUM THERAPY OF SEPTIC MENINGITIS

Following Lamar's [9] report on the successful treatment of experimental type I pneumococcus meningitis of monkeys with intraspinal injections of mixtures of type I serum with boric acid and sodium oleate, hopes were entertained for success in the treatment of type I infections of human beings, but such has not been realized in my own experience with four subjects treated with these mixtures. Idzumi and I also

9. Lamar: J. Exper. Med. **16**:581, 1912.

failed to influence materially the course and mortality of experimental pneumococcus meningitis of rabbits with these mixtures or the serum alone, and similar negative results were observed in the present series of investigations.

The intramuscular, intravenous, intracisternal and intraventricular injection of polyvalent antistreptococcus serum, including a concentrated serum, has failed to influence appreciably or constantly the course and mortality of meningitis of dogs, produced by intracisternal injections of our culture of highly virulent hemolytic streptococcus.

The same has been true in the treatment of experimental meningitis of dogs produced by intracisternal injections of virulent type I pneumococci, and treated with intramuscular, intravenous, intracisternal and intraventricular injections of stock polyvalent or type I antipneumococcus serum.

But so far as the treatment of pneumococcus meningitis is concerned, I believe that the subthecal injection of pneumococcus antibody solution offers far more hope for success than antipneumococcus serum. To the best of my knowledge, this product was first used by Wieder [10] in the treatment of a patient with pneumococcus meningitis who was in the Polyclinic Hospital several years ago; a rapid influence on the organisms, along with prolongation of life, convinced him that a favorable influence was produced, although the patient subsequently died with an unsuspected abscess of one of the frontal lobes of the brain. Subsequently, I employed antibody solution by intralumbar and intramuscular injection in the treatment of a boy, aged 10 years, who was severely ill with pneumococcus meningitis complicating pneumococcus otitis media. He recovered sufficiently to be up and about, only to succumb about four weeks later with an abscess of the cerebellum. I have also used antibody solution in the treatment of meningitis in a child of one of my colleagues. The condition was alleged to be one of pneumococcus infection, but I could not find any pneumococci in the spinal fluid; the child made a complete recovery. Ervin [11] has recorded the recovery of a patient, an adult, with pneumococcus meningitis without preceding primary infection of the mastoid or accessory sinuses, following intraspinal and intramuscular injections of antibody solution, the bacteriologic diagnosis having been made by Dr. Robert A. Keilty, a pathologist and bacteriologist. It would appear, therefore, that this product holds out some promise for success in the treatment of pneumococcus meningitis, and this impression has gained some confirmation in the results of our experiments in the treatment of experimental pneumococcus meningitis of dogs. It is true,

10. Wieder, H. S.: Laryngoscope **34**:609 (Aug.) 1924.
11. Ervin, C. E.: Atlantic M. J. **28**:590, 1925.

however, that intramuscular, intravenous, intracisternal and intraventricular injections of antibody solution alone have not saved the lives of any of our animals, but the duration of the lives of several has been prolonged for a few days, and when administered along with lavage of the ventricles to the cisterna magna, complete recoveries have occurred. This would appear to be a particularly desirable product for the treatment of meningitis when it is so desirable to inject subthecally as powerful a product as possible in the least bulk of fluid.

LAVAGE AND DRAINAGE IN THE TREATMENT OF SEPTIC MENINGITIS

Without attempting a complete review of the literature on pneumococcus and streptococcus meningitis, I believe it may be stated that in the great majority of cases intraspinal treatment alone has failed, although the institution of surgical drainage by laminectomy, as recommended by Hill,[12] or of the cisterna magna, as practiced by Dandy,[13] has resulted in some recoveries during the past fifty years, as recently reviewed by Rainey and Alford.[14] They have also recorded the recovery of two patients with septic meningitis by the institution of continuous spinal drainage. Certainly it is one of the outstanding and clearest conclusions of our experimental study that drainage alone, or drainage with lavage, constitutes the most important phase of treatment, and it is earnestly hoped that there will be a wider and clearer realization of the fact that pneumococcus and streptococcus meningitis are surgical problems demanding the institution of much better drainage and treatment than afforded by merely one or two spinal punctures a day with the intraspinal injection of an antiserum. Dandy, for example, has been able to save three out of a series of four cases of septic meningitis caused by staphylococci and streptococci, by continuous drainage from the cisterna magna, and although so high an authority as Eagleton [15] states that subarachnoid irrigation is impossible for mechanical reasons and drainage of the system fallacious, yet I believe that drainage from the cisterna magna as described by Dandy is worthy of serious consideration, even though subdural irrigation, as originally advised by Eagleton, has since been abandoned by him.

In our experiments, the only effective method of treatment found so far in the treatment of severe streptococcus and pneumococcus leptomeningitis of dogs has been trephining and washing one or both ven-

12. Hill, R.: Laminectomy for Meningitis, J. A. M. A. **76**:267 (Jan. 22) 1921.
13. Dandy, W. E.: Surg. Gynec. & Obst. **39**:760 (Dec.) 1924.
14. Rainey, W. R., and Alford, L. B.: The Treatment of Septic Meningitis by Continuous Drainage, J. A. M. A. **81**:1516 (Nov. 3) 1923.
15. Eagleton, Wells P.: The Surgical Treatment of Meningitis, J. A. M. A. **83**:1900 (Dec. 13) 1924.

tricles through to the cisterna magna with warm saline or Ringer's solution, escape of the fluid being provided for by the insertion of a needle into the cisterna magna. One treatment alone of this kind has saved animals when the untreated controls have all died in the usual time of four to seven days. Sometimes pus continued to drain from the trephine opening for a few days, and these animals usually fared better than those without this drainage; we believe that lavage alone is full of great promise in the treatment of septic meningitis of human beings, provided treatment is instituted sufficiently early in the disease. We have been able to save dogs by this means after the onset of symptoms but before the exudate became too purulent and plastic. It is possible that washing the spinal subarachnoid space between the cisterna magna and the lower lumbar region of the cord would improve the results, but we have not found this necessary in the treatment of these experimental infections. The introduction of an immune serum or pneumococcus antibody solution following lavage might also improve the results, but lavage alone has proved effective.

RECOMMENDATIONS IN THE TREATMENT OF SEPTIC MENINGITIS

In the treatment of streptococcus and pneumococcus meningitis of otitic or nasal origin, I believe, therefore, that it is essential to make the diagnosis as early as possible and institute treatment without delay. It is true that early spinal puncture and examination of the cerebrospinal fluid are generally required, and that the physician may naturally hesitate to conduct spinal puncture by reason of the observations of Weed and his associates [16] that meningitis of cats has been produced by withdrawal of spinal fluid when *B. mucosus-capsulatus, B. pyocyaneus* or *B. paratyphosus B.* were present in the blood, but I believe this danger has been greatly overestimated so far as meningitis of human beings is concerned. I have never been able to localize streptococci or pneumococci from the blood to the meninges of rabbits or dogs by simple spinal puncture, although setting up a mild meningeal irritation by the intraspinal injection of normal serum has sometimes had this effect. But I feel confident that the slow and careful removal of a few cubic centimeters of cerebrospinal fluid from a child or an adult suspected of having meningitis will do no harm either in the way of favoring the localization of organisms in the meninges from the blood, or by favoring the extension of a localized meningitis, and that this kind of spinal puncture should be resorted to early for diagnostic purposes.

16. Weed, L. H.; Wegeforth, Paul; Ayer, J. B., and Felton, Lloyd: The Production of Meningitis by Release of Cerebrospinal Fluid, J. A. M. A. **72**:190 (Jan. 18) 1919.

If the fluid is found clear, one would naturally hesitate to inject anything subthecally, although it is well, in my opinion, to inject antibody solution intravenously or subcutaneously in cases of suspected pneumococcus meningitis, or mercurochrome or gentian violet intravenously in suspected streptococcus infections.

If a purulent fluid is recovered, indicating the presence of a widespread leptomeningitis, I believe the case should be regarded at once as one for surgery, calling for the drainage of the local focus of infection if present or discoverable, the performance of trephining and puncture of a ventricle, along with puncture of the cisterna magna and lavage from the ventricles to the cistern. We have usually washed out the dogs with 20 to 40 cc. of warm saline or Ringer's solution, and never observed any ill effects. Lavage from the cistern to the lumbar region of the cord may be done at the same time, although I am convinced that septic meningitis kills from the cistern upward rather than by spinal meningitis. Washing out the ventricle on the infected side of the head is recommended, although in severe cases both ventricles may require irrigation. In pneumococcus infections, lavage may be followed by the introduction of pneumococcus antibody solution in dose of about 0.5 cc. for each 2 pounds of weight. Whether or not several treatments of this kind will be required I am unable to state; that, doubtless, will depend on the clinical status of each individual case; but with infected dogs one treatment has usually sufficed. At all events, I hope that surgeons will not hesitate to institute treatment along these lines under ether anesthesia, particularly in view of the fairly well established clinical and experimental fact that ordinary treatment by spinal puncture and intraspinal medication is almost sure to fail.

Possibly the institution of continuous drainage from the cisterna magna or lower spinal subarachnoid space, with or without subdural or ventricular irrigation will prove to be a better method, but I hope later to be able to report the results of experiments now in progress along these lines.

II. ETHYLHYDROCUPREIN HYDROCHLORIDE IN THE TREATMENT OF PNEUMOCOCCUS MENINGITIS

WITH THE ASSISTANCE OF

ANNA M. RULE AND BERNARD MADDEN

The high and selective bactericidal activity of ethylhydrocuprein hydrochloride (optochin) for pneumococci in vitro, even in the presence of pus and other proteins, along with a slight but definite protective and curative activity in experimental pneumococcus infections of mice and rabbits, has been the basis of the hope that it may prove efficacious in the treatment of pneumococcus meningitis. First synthesized by

Morgenroth and Levy [17] in 1911 from hydroquinine and designated as "optochin" (best quinine), now marketed under the name of "numoquin," it has proved useful in the treatment of pneumococcus infections of the eye and other localized infections by direct application, although generally regarded as too toxic for use in the treatment of pneumonia.

Its high pneumococcidal activity in vitro has led to the hope that it may be possible to introduce sufficient optochin into the subarachnoid space in pneumococcus meningitis to secure bactericidal effects without added irritation of the meninges or systemic toxic effects. Thus, in 1920, Idzumi and I [18] observed that equal parts of 1:1,000 solution of ethylhydrocuprein and purulent spinal fluids containing type I or type II pneumococci usually resulted in the complete destruction of the organisms in about thirty minutes at 37 C., while final dilutions of 1:4,000 were bactericidal in an hour. We also found that while 0.03 to 0.05 Gm. per kilogram of body weight of rabbits injected intraspinally produces a fatal leptomeningitis in forty-eight hours, the compound was well borne in dose of 0.5 cc. of 1:1,000 solution (0.0005 Gm.) per kilogram, and produced no evidences of leptomeningitis even by repeated intraspinal injection.

It was hoped, therefore, that sufficient amounts of ethylhydrocuprein could be injected intraspinally to raise the bactericidal activity of the spinal fluid to a therapeutic threshold without producing toxic effects or retarding phagocytosis. The results of experiments with pneumococcus meningitis of rabbits showed that when 0.5 cc. of 1:500 to 1:1,000 solutions per kilogram were injected intraspinally not later than four to six hours after infection, slightly curative effects were sometimes observed, although when the infection was highly virulent the drug had practically no effect, as likewise when the administration was delayed twenty-four hours or longer. Mixtures of ethylhydrocuprein and homologous antipneumococcus serum or mixtures of the drug, serum and sodium oleate did not yield better results, than the drug alone; however even though the curative effects were but slight at best, we believe that the daily or twice daily withdrawal of spinal fluid, followed by the intraspinal injection of 15 to 20 cc. of 1:500 to 1:1,000 solutions in saline solution may prove of aid in the treatment of pneumococcus meningitis of human beings.

My clinical experience with this method in the treatment of eleven cases of pneumococcus meningitis during the past six years has not been at all encouraging. All of these cases were of otitic origin and severe infections. In three of the patients, however, life was certainly prolonged, and in one even hope for recovery was for a time entertained.

17. Morgenroth and Levy: Berl. klin. Wchnschr. **48**:1560 and 1970, 1911.
18. Idzumi, G., and Kolmer, J. A.: Footnote 4.

I believe that recoveries have been credited to the administration of ethylhydrocuprein, but chiefly in cases of pneumococcus meningitis developing during pneumonia, in which spontaneous recovery is possible and the prognosis much better than in cases developing secondary to primary otitic or nasal infections, in which the mortality is practically 100 per cent. It is in these cases that I have used ethylhydrocuprein by intraspinal injection, combined in some cases by intravenous injection followed by oral administration to raise the bactericidal activity of the blood.

In the course of the present investigation, I thought it worth while to experiment again with ethylhydrocuprein hydrochloride in the treatment of type I pneumococcus meningitis of dogs. Severe infections, usually fatal in five to seven days, were produced by injecting, under ether anesthesia, 0.1 cc. of 1:60 to 1:100 dilutions of twenty-four hour hormone broth cultures into the cisterna magna per kilogram of body weight. Almost invariably, symptoms of meningitis were apparent

TABLE 1.—*Ethylhydrocuprein Hydrochloride in the Treatment of Experimental Pneumococcus Meningitis of Dogs**

Route of Administration	Dose per Kilogram, Gm.	First Dose after Infection	Subsequent Daily Treatments	Survival, Days
Intravenously	0.005	24 hours later	3	4†
Intravenously	0.005	24 hours later	3	5†
Intracisternally	0.0002	24 hours later	2	4†
Intracisternally	0.0002	24 hours later	3	7†
Untreated control	—	—	—	5†
Untreated control	—	—	—	6†

* Infected by the intracisternal injection of 0.1 cc. of 1:100 dilution of twenty-four hour hormone broth culture of type I pneumococcus.
† Cultures of heart blood sterile.

within thirty-six hours, along with cloudy spinal fluids containing pus cells and myriads of cocci. At necropsy, a diffuse purulent leptomeningitis was found, with pus in both lateral ventricles.

In view of the fact that the treatment of human beings is not instituted until some symptoms of meningitis are apparent, we did not begin the administration of ethylhydrocuprein for at least twenty-four to thirty-six hours after infection when slight symptoms were present. In some experiments, treatment was delayed several days to duplicate still further conditions encountered in practice.

A large number of dogs were used, but the results shown in tables 1, 2 and 3 indicate the methods of administration, and serve as examples of the results observed. All intracisternal and intraventricular injections were done under ether anesthesia, and the animals subsequently kept under morphine to prevent pain. When given intracisternally or intraventricularly, the dose was contained in a total of 0.5 to 1.0 cc. for dogs weighing from 5 to 10 Kg.

As shown in table 1, the daily intravenous injection of ethylhydrocuprein in dose of 0.005 Gm. per kilogram had no appreciable effect on the duration and mortality of the disease. Daily puncture of the cisterna magna with drainage of spinal fluid, followed by the injection of 0.0002 Gm. per kilogram of weight, was likewise without effect. The latter corresponds to the injection of 12 to 15 cc. of a 1 : 1,000 solution per 60 Kg., or approximately 130 pounds. Slightly more may be injected intraspinally, but this dose proved about the maximum for intracisternal administration.

We have also administered the drug by intraventricular injection in the same dose, sometimes combined with intravenous or intramuscular injections, but likewise with negative results, as shown in table 2, summarizing one experiment of this kind. It is true that the lives of some

TABLE 2.—*Ethylhydrocuprein Hydrochloride in the Treatment of Experimental Pneumococcus Meningitis of Dogs**

Dose and Administration, Gm. per Kg.	First Treatment after Infection	Subsequent Daily Treatments	Survival, Days	Necropsy
0.0002 intraventricularly 0.010 intravenously	24 hours; no symptoms	2	6	Ventricle clear; cerebral and spinal
0.0002 intraventricularly 0.010 intramuscularly	2 days symptoms	1	4	Ventricle pus; cerebral and spinal
0.0002 intraventricularly	24 hours; no symptoms	2	6	Ventricle clear; cerebral and spinal
0.0002 intraventricularly	2 days symptoms	1	3	Ventricle pus; cerebral and spinal
0.010 intramuscularly 0.010 intravenously	24 hours; no symptoms	2	4	Ventricles pus; cerebral and spinal
Untreated control	—	—	4	Ventricles pus; cerebral and spinal

* Infected by the intracisternal injection of 0.1 cc. per kilogram of 1:60 dilution of twenty-four hour hormone broth culture of pneumococcus type I.

dogs were apparently prolonged by one or two days, but these occurrences may have been due to other factors and notably to a higher immunologic resistance of some animals.

Somewhat more encouraging results were observed at times, when the administration of ethylhydrocuprein was combined with pneumococcus antibody solution, as shown in the results of some experiments in table 3. We injected the drug in the same dose intraventricularly, with 0.2 cc. of antibody solution per kilogram of body weight, and in some experiments, in addition, gave ethylhydrocuprein or antibody solution by intravenous or intramuscular injection. Occasionally, the lives of some dogs were unquestionably prolonged for a few days, but we believe these results were due more to the influence of the antibody solution than to the drug. Negative results were observed with type 1 antipneumococcus serum, as will be reported on separately.

I believe it may be stated, therefore, that the daily intraspinal, intracisternal and intraventricular administration of ethylhydrocuprein in

dose approximating 0.0002 Gm. per kilogram, or about 15 cc. of a 1 : 1,000 solution per 130 pounds, is without effect in the treatment of acute pneumococcus meningitis. At least this has been my clinical experience in the treatment of cases of otitic origin. The results of the experiments briefly summarized herein also show that the drug is without or almost without effect in the treatment of severe experimental infections when the first dose is delayed until early symptoms have appeared; in mild experimental infections, somewhat better results are sometimes observed when treatment is instituted within a few hours after infection of the meninges.

Ethylhydrocuprein, however, is undoubtedly highly destructive for the pneumococcus in spinal fluid under certain conditions. When given intraventricularly, we sometimes observed much less infection in the injected ventricle than in the cerebral and spinal subarachnoid spaces. I

TABLE 3.—*Treatment of Experimental Pneumococcus Meningitis of Dogs with Antibody Solution and Ethylhydrocuprein (Optochin) Hydrochloride* *

Treatment	First Treatment after Infection	Subsequent Daily Treatments	Survival, Days	Necropsy
0.0002 Gm. optochin intraventricularly 0.2 cc. antibody intraventricularly	48 hours; symptoms	3	8	Accidental death; no meningitis
0.0002 Gm. optochin intraventricularly 0.2 cc. antibody intraventricularly	48 hours; symptoms	2	7	Ventricles clear; cerebral and spinal
0.0002 Gm. optochin intraventricularly 0.2 cc. antibody intraventricularly 0.010 Gm. optochin intramuscularly	48 hours; symptoms	1	4	Ventricles pus; cerebral and spinal
0.0002 Gm. optochin intraventricularly 0.2 cc. antibody intraventricularly 2.0 cc. antibody intravenously 0.010 Gm. optochin intramuscularly	48 hours; symptoms	2	6	Ventricles clear; cerebral and spinal
Untreated control.....	48 hours; symptoms	—	4	Ventricles pus; cerebral and spinal

* Infected by the intracisternal injection of 0.1 cc. of 1:60 dilution of twenty-four hour hormone broth culture of type I pneumococcus.

believe that the drug is capable of destroying some pneumococci, although it is likely to undergo high dilution soon after injection, with a reduction of bactericidal activity below a therapeutic threshold. When injected intraspinally, it may readily enough destroy some pneumococci at or near the site of administration before high dilution or absorption has occurred. Unfortunately, there are reasons for believing that the highly plastic nature of the pneumococcus exudate soon reduces or completely obstructs the diffusion of ethylhydrocuprein introduced by intraspinal injection and to a lesser extent by intracisternal or intraventricular injection. However, when administered after lavage by injecting saline or Ringer's solution into one of the lateral ventricles and providing for its escape by means of a needle introduced into the cisterna magna, followed by the intraventricular and intracisternal injection of ethylhydrocuprein, much better results have been secured.

due in large part to the lavage rather than to the drug, since lavage alone yielded similar results. These experiments are being separately described.

SUMMARY

1. The daily intraspinal, intracisternal or intraventricular injection of ethylhydrocuprein hydrochloride in dose of 0.0002 Gm. per kilogram had no appreciable curative effects in the treatment of acute experimental pneumococcus meningitis of dogs. This dose corresponds to from 12 to 18 cc. of a 1 : 1,000 solution per 60 kilograms, or about 130 pounds.

2. No better results were secured by combining these routes of administration with the intravenous or intramuscular injections of the compounds.

3. Combined treatment with antipneumococcus serum and ethylhydrocuprein did not improve the results, although some improvement was noted in combined treatment with pneumococcus antibody solution.

4. Especially good results were secured by lavage from the ventricles to the cisterna magna, followed by intraventricular and intracisternal injections of the drug, but lavage alone has yielded similar results.

III. MERCUROCHROME-220 SOLUBLE IN THE TREATMENT OF PNEUMOCOCCUS AND STREPTOCOCCUS MENINGITIS

WITH THE ASSISTANCE OF

ANNA M. RULE AND BERNARD MADDEN

Mercurochrome-220 soluble has been so widely employed in the treatment of bacteremias by intravenous injection, and of localized bacterial infections by topical application, that we thought it advisable to employ the compound in the treatment of experimental septic meningitis by intravenous and subthecal injection. Its toxicity for the meninges and relatively low bactericidal activity for pneumococci and streptococci in purulent spinal fluids, however, soon indicated to us that it may not be possible to introduce sufficient amounts intraspinally, intracisternally or intraventricularly to influence the disease materially, and the results of actual experiments soon confirmed this expectation.

The compound has been used to some extent clinically in the treatment of septic meningitis, but generally with negative results. In at least one instance brought to our attention, a gross error in dosage occurred when 20 cc. of a 1 per cent solution, the usual full dose for an adult by intravenous injection, was injected intraventricularly with a promptly lethal result. As previously mentioned, Adams [19] gave intravenous injections to one patient with pneumococcus meningitis, but without success; Young, Hill and Scott [20] report the treatment of five additional cases by Schwartz, Tyler and Berghausen, with the recovery

19. Adams, D. S.: Footnote 6.
20. Young, H. H.; Hill, J. H., and Scott, W. W.: Footnote 5.

of two patients, which may or may not have been due to intravenous injections of the drug.

Toxicity of Mercurochrome by Subthecal Injection.—The maximum single tolerated dose of mercurochrome for dogs by intravenous injection is about 0.035 Gm. per kilogram, corresponding to 3.5 cc. of a 1 per cent solution. When injected intraspinally, the maximum single tolerated dose is about 0.001 to 0.003 Gm. per kilogram, corresponding to 1 to 3 cc. of a 1 : 1,000 or 0.1 per cent solution. While these amounts are ordinarily well borne by normal dogs by this route as well as by intracisternal and intraventricular injection, yet mild degrees of meningeal irritation may result, especially characterized by erythrocytic exudation as found by Idzumi and me,[21] following intraspinal injections of sodium-oxymercury-orthonitrophenolate to rabbits. But when repeated subthecal injections are given dogs with acute meningitis, the tolerance is much less, since resistance is reduced by the infection; under these circumstances we have generally found it necessary to drop down to doses of 0.0001 to 0.0003 Gm. per kilogram, corresponding to 0.1 to 0.3 cc. of 1 : 1,000 solutions. For the treatment of septic meningitis of human beings, we believe that the dose by subthecal injection may be from 6 to 18 cc. of a 1 : 1,000 solution (not 1 : 100) for subjects of approximately 130 pounds in weight.

Bactericidal Activity of Mercurochrome in Purulent Spinal Fluid.—The bactericidal activity of mercurochrome in vitro for pneumococci and streptococci in purulent spinal fluids has varied considerably with different fluids, doubtless influenced by the number and condition of the organisms present and amounts of pus cells and dissolved proteins in the fluids. In general terms, however, equal parts of mercurochrome solution 1 : 300 and of spinal fluid giving a final dilution of 1 : 600 has proved completely bactericidal for both organisms in five minutes at 37 C. The range of final bactericidal dilutions with both organisms has varied from 1 : 400 to about 1 : 1,000 under similar conditions.

When it is remembered that in the treatment of septic meningitis the daily amounts injected subthecally can seldom be more than 0.0001 to 0.0003 Gm. per kilogram, there is little or no reason for expecting beneficial results because of dilution beyond the bactericidal threshold, and the results of numerous experiments have shown this to be the case.

Mercurochrome in the Treatment of Septic Meningitis.—In our early experiments, white rats were infected by direct subdural (cerebral) injections of 0.1 cc. of 1 : 15,000,000 dilution of our strain of hemolytic streptococcus. Severe meningitis usually resulted in twenty-four to forty-eight hours, with death in about four days. The intravenous injection of mercurochrome in dose of 0.005 Gm. per kilogram had no

21. Idzumi, G., and Kolmer, J. A.: Footnote 4.

appreciable effect, and subdural injections of 0.0001 Gm. per kilogram were likewise ineffective. The results of one experiment of this kind are shown in table 4, and while a rat occasionally survived, yet this sometimes happened with untreated controls, probably due to the escape of small amounts of culture at the time of infection or to exceptionally high instances of immunologic resistance.

A septic meningitis of rabbits was also produced by the intracisternal injection of a virulent culture of *Staphylococcus pyogenes-aureus,* which was usually fatal in untreated controls in four to seven days. Treatment with mercurochrome in dose of 0.005 to 0.008 Gm. per kilogram

TABLE 4.—*Mercurochrome-220 Soluble in the Treatment of Experimental Streptococcus Meningitis of Rats* *

Route of Administration	Dose per Kilogram, Gm.	First Dose after Infection	Number of Subsequent Daily Doses	Survival, Days
Intravenously	0.005	4 hours later	2	4†
Intravenously	0.005	4 hours later	3	4†
Intravenously	0.010	4 hours later	2	5†
Intravenously	0.010	4 hours later	3	4†
Subdurally	0.0001	4 hours later	2	Lived indefinitely
Subdurally	0.0001	4 hours later	3	4†
Untreated control	—	—	—	3†
Untreated control	—	—	—	4†

* Infected by subdural injection of 0.1 cc. of 1:15,000,000 dilution of twenty-four hour hormone broth culture.
† Showed streptococci in cultures of heart blood.

TABLE 5.—*Mercurochrome in the Treatment of Experimental Staphylococcus Meningitis of Rabbits* *

Route of Administration	Dose per Kg., Gm.	Number of Daily Doses	Survival Days
Intravenously	0.008	5	8*
Intravenously	0.008	3	4*
Intravenously	0.008	8	Lived indefinitely
Intracisternally	0.0001	2	3*
Intracisternally	0.0001	2	3*
Intracisternally	0.0001	2	3*
Untreated control	—	—	6*
Untreated control	—	—	4*

* Cultures of heart blood sterile.

by intravenous injection, or 0.0001 to 0.0002 Gm. per kilogram by intracisternal injection, was generally without appreciable effect, although occasionally an animal survived a day or two beyond the untreated controls, as shown in table 5.

Numerous dogs were infected under ether anesthesia by intracisternal injections of 0.1 cc. of 1:60 to 1:100 dilutions of twenty-four hour hormone broth cultures of our strain of type I pneumococcus. Symptoms were usually present in about thirty-six hours, followed by death in four to six days. The intravenous injection of mercurochrome in dose of 0.003 to 0.008 Gm. per kilogram had no effect, and the intracisternal injection of 0.0001 to 0.0002 Gm. per kilogram was likewise

ineffective so far as duration of life was concerned, as shown in table 6. However, when given by intraventricular injection, we sometimes noted on necropsy that the injected ventricle was stained and free of pus, while pus was elsewhere present in the subarachnoid space. This indicates that mercurochrome is capable of effecting local sterilization, although it was not possible in our experiments to introduce sufficient amounts to prolong appreciably the lives of dogs beyond the range of the untreated controls. All injections were made under ether anesthesia.

Similar results were observed in the treatment of experimental streptococcus meningitis of dogs, as shown in tables 7 and 8. Animals were infected under ether anesthesia by intracisternal injections of our highly virulent strain of hemolytic streptococcus, and symptoms were generally apparent in three to five days. When treatment was begun at this time, the intravenous injection of 0.005 to 0.008 Gm. of mercurochrome was without effect, as likewise when treatment was started twenty-four hours after infection and before symptoms developed (table 8). Intraven-

TABLE 6.—*Mercurochrome in the Treatment of Experimental Pneumococcus Meningitis of Dogs* *

Route of Administration	Dose per Kilogram, Gm.	First Dose after Infection	Number of Subsequent Daily Doses	Survival, Days
Intravenously	0.0033	24 hours later	2	4†
Intravenously	0.005	24 hours later	2	3†
Intracisternally	0.0001	24 hours later	2	5†
Intracisternally	0.0001	24 hours later	3	5†
Untreated control	—	—	—	5†
Untreated control	—	—	—	6†

* Infected by intracisternal injection of 0.1 cc. of 1:100 dilution of twenty-four hour hormone broth culture of type I pneumococcus.
† Cultures of heart blood sterile.

tricular injections of mercurochrome in dose of 0.0002 to 0.0003 Gm. per kilogram were likewise ineffective, even when the first doses were administered twenty-four hours after infection. On necropsy, however, we sometimes observed that the injected ventricle was stained and free of pus, while pus was found widely distributed elsewhere in the subarachnoid space.

The results of our experiments, therefore, have not given us any hope for success in the treatment of streptococcus and pneumococcus meningitis of human beings by the intravenous or subthecal injection of mercurochrome. It is possible, though, that intravenous injections of the maximum dose may prove of aid in association with serum therapy for the treatment of the bacteremia (septicemia) sometimes associated with meningitis, but we doubt if anything worth while is to be gained by the subthecal injection of the drug. If employed by this route of injection, great care must be exercised in dosage, and in our opinion should not exceed 6 to 15 cc. of a 1 : 1,000 solution (not 1 : 100) per 60 kilograms of body weight.

SUMMARY

1. The maximum tolerated dose of mercurochrome for normal dogs by subthecal injection is approximately 0.001 to 0.002 Gm. per kilogram of body weight, corresponding to 1 to 2 cc. of a 1:1,000 solution per kilogram. The tolerance of dogs with streptococcus or pneumococcus meningitis is less, and by repeated injections the maximum tolerated dose was found to be from 0.0001 to 0.0003 Gm. per kilogram. In the treatment of meningitis by intraspinal, intracisternal or intraventricular injection of mercurochrome, these doses would correspond to 6 to 18 cc.

TABLE 7.—*Mercurochrome in the Treatment of Experimental Streptococcus Meningitis of Dogs**

Route of Administration	Dose per Kg., Gm.	First Dose after Infection	Subsequent Daily Doses	Survival, Days	Necropsy
Intraventricularly	0.0002	24 hours; no symptoms	1	5	Ventricles pus; cerebral and spinal
Intraventricularly	0.0003	24 hours; no symptoms	2	6	Ventricle clear; cerebral and spinal
Intraventricularly	0.0002	4 days; symptoms	2	6	Ventricles pus; cerebral and spinal
Intraventricularly	0.0003	4 days; symptoms	2	6	Ventricle clear; cerebral and spinal
Untreated control	—	—	—	5	Ventricles pus; cerebral and spinal

* Infected by the intracisternal injection of 0.1 cc. of 1:5 dilution of twenty-four hour hormone broth culture.

TABLE 8.—*Mercurochrome in the Treatment of Experimental Streptococcus Meningitis of Dogs**

Route of Administration	Dose per Kilogram, Gm.	First Dose after Infection	Number of Subsequent Daily Doses	Survival, Days
Intravenously	0.005	24 hours later	3	6†
Intravenously	0.005	24 hours later	4	5†
Intracisternally	0.0001	24 hours later	2	6†
Intracisternally	0.0001	24 hours later	3	5†
Untreated control	—	—	—	5†
Untreated control	—	—	—	6†

* Infected by the intracisternal injection of 0.1 cc. of 1:5 dilution of twenty-four hour hormone broth culture.
† Cultures of heart blood sterile.

of a 1:1,000 solution (not 1:100) for an adult human being of approximately 130 pounds weight.

2. The bactericidal activity of mercurochrome for pneumococci and streptococci in purulent cerebrospinal fluids was found to be, in final dilutions, varying from 1:400 to 1:1,000 in an exposure of five minutes at 37 C. In view of the small amounts that may be safely administered by subthecal injection, it would not appear possible, therefore, to secure sufficient bactericidal effects in the subarachnoid space to influence the disease materially.

3. Mercurochrome in dose of 0.005 to 0.008 Gm. per kilogram by intravenous injection was without appreciable effect in the treatment of streptococcus meningitis of rats, staphylococcus meningitis of rabbits, and streptococcus and pneumococcus meningitis of dogs. Subdural and intracisternal injections of the compound in doses varying from 0.0001 to 0.0003 Gm. per kilogram were likewise ineffective in the treatment of these various kinds of experimental septic meningitis.

4. Mercurochrome by intravenous injection of maximum amounts may aid in removing bacteremia (septicemias), but is believed to be without curative properties in the treatment of the meningeal lesions of septic meningitis.

IV. GENTIAN VIOLET, ACRIFLAVINE AND RIVANOL IN THE TREATMENT OF PNEUMOCOCCUS AND STREPTOCOCCUS MENINGITIS

WITH THE ASSISTANCE OF
ANNA M. RULE AND BERNARD MADDEN

Gentian violet and neutral acriflavine have been employed so widely in the treatment of bacteremias (septicemias) by intravenous injection, and in the treatment of localized infections by topical application, especially in infections by the gram-positive organisms like staphylococci, streptococci and pneumococci, that we have approached the treatment of experimental septic meningitis with these dyes with considerable interest and anticipation of some success. Unfortunately, however, they have not yielded very encouraging results when employed alone in the treatment of experimental pneumococcus and streptococcus meningitis of dogs, although better results were observed when used after lavage and in conjunction with serum therapy.

Rivanol,[7] a new acridine derivative 2-ethoxy-6, 9-diamino-acridine-ochlorate, was prepared by Morgenroth, Schnitzer and Rosenberg,[22] and has been found somewhat curative for experimental streptococcus infections of mice. It has been employed in Germany for the treatment of streptococcus bacteremia, being injected intravenously in doses of 15 to 30 cc. of 1 : 1,000 solution for adults of average weight. Rivanol has also been employed in 1 : 1,000 solutions for the treatment of local infections, and for these reasons we have considered worth while employing the compound in the treatment of experimental streptococcus meningitis.

The only case of meningitis of which we have knowledge in which gentian violet was employed in treatment by subthecal injection, is that of a streptococcus infection in a boy, aged 2 years, reported by Royster.[23] The dye was administered by intraspinal injection in doses varying from

22. Morgenroth, I.; Schnitzer, R., and Rosenberg, E.: Deutsche med. Wchnschr. **47**:1317 (Nov. 3) 1921.
23. Royster, L. T.: Footnote 8.

0.00004 to 0.00012 Gm., about 16 injections in all being given. The child lived about three weeks, and Dr. Royster believed that the prolongation of life was due to the treatment given. The doses, however, were somewhat small, and possibly a better result would have followed the injection of larger amounts.

Toxicity of Gentian Violet, Acriflavine and Rivanol by Subthecal Injection.—The toxicity of these dyes by intravenous injection into white rats, rabbits and dogs has varied considerably according to their chemical purity, which probably largely accounts for rather widely varying reports by different investigators. We have employed the gentian violet prepared by Coleman and Bell, the neutral acriflavine prepared by the National Anilin and Chemical Company and the rivanol by Meister, Lucius and Bruning, Hoechst.

By intravenous injection to rats, using 1 per cent solutions injected at the rate of 2 cc. per minute, the maximum tolerated doses (three weeks) have been approximately as follows:

Gentian violet	0.125 Gm. per kilo.
Acriflavine	0.035 Gm. per kilo.
Rivanol	0.016 Gm. per kilo.

By injection into the cisterna magna of rabbits, the maximum tolerated doses have been approximately as follows:

Gentian violet	0.001 to 0.003 Gm. per kilo.
Acriflavine	0.002 to 0.003 Gm. per kilo.
Rivanol	0.0005 to 0.001 Gm. per kilo.

But the tolerance of rabbits and dogs with acute streptococcus and pneumococcus meningitis is much less, and the doses must be smaller if repeated intraspinal, intracisternal or intraventricular injections are given. In our experience, the usual tolerated dose of all three dyes by these routes of administration was from 0.0001 to 0.0003 gm. per kilogram. These amounts correspond approximately to 0.006 to 0.018 Gm. per 130 pounds, or from 6 to 18 cc. of 1:1,000 solutions.

Bactericidal Activity of Gentian Violet, Acriflavine and Rivanol for Staphylococci, Pneumococci and Streptococci in Purulent Spinal Fluids.—In our experience, the bactericidal activity of these dyes has not been as high as frequently stated in the literature. When equal parts of solution of dye and purulent spinal fluid were kept at 37 C., and subcultured after a contact of five minutes, the completely bactericidal final dilutions of dye were approximately 1:1,800 to 1:4,000 for all three organisms, the results varying according to several factors, among which the numbers and vitality of cocci, numbers of pus cells and amounts of dissolved proteins in the purulent fluids were of most importance.

When it was found that only 0.0001 to 0.0003 Gm. per kilogram of weight could be repeatedly injected subthecally in the treatment of

experimental septic meningitis, we almost abandoned hope for meeting with success in the treatment of these severe, experimentally produced infections.

Gentian Violet in the Treatment of Experimental Staphylococcus Meningitis of Rabbits.—Our first experiments were conducted with rabbits infected by intracisternal injections of a virulent culture of *Staphylococcus pyogenes-aureus.* The intravenous injection of gentian violet in dose of 0.005 Gm. per kilogram was without appreciable effect, even when the first dose was given twenty-four hours after infection and just before the onset of symptoms.

The intracisternal injection of 0.0002 Gm. per kilogram apparently prolonged the lives of a few animals by a day or two, as shown in the results of one experiment summarized in table 9, but on the whole the results were of a negative character.

TABLE 9.—*Gentian Violet in the Treatment of Experimental Staphylococcus Meningitis of Rabbits*

Route of Administration	Dose per Kg., Gm.	Number of Daily Doses	Survival Days
Intravenously	0.005	6	7*
Intravenously	0.005	8	Lived indefinitely
Intravenously	0.005	3	3*
Intracisternally	0.0002	2	4*
Intracisternally	0.0002	4	6*
Intracisternally	0.0002	5	7*
Untreated control	—	—	6*
Untreated control	—	—	4*

* Cultures of heart blood sterile.

Gentian Violet in the Treatment of Experimental Streptococcus Meningitis.—White rats were infected by subdural injections of our highly virulent strain of hemolytic streptococcus, and treatment was instituted from one to three days later. Intravenous injections of gentian violet in doses varying from 0.005 to 0.008 Gm. per kilogram were apparently without effect, as likewise subdural injections of 0.0001 to 0.0002 Gm. per kilogram, administered on the same side of the head as the cocci. The results of one of these experiments are shown in table 10 as an example of the whole.

Similar negative results were observed in the treatment of dogs infected by intracisternal injections of the same streptococcus. Treatment was started about twenty-four hours later, and in others delayed for about four days when symptoms of meningitis usually appeared. The intravenous injection of gentian violet in dosage of 0.005 Gm. per kilogram was without appreciable effect even when repeated at daily intervals.

The repeated intracisternal injections of 0.0001 to 0.0002 Gm. per kilogram under ether anesthesia were likewise ineffective, as shown in the results of one experiment in table 11. Intraventricular injections

under ether anesthesia of 0.0003 to 0.0004 Gm. per kilogram were also ineffective, so far as duration of the lives of the animals was concerned, but we sometimes observed deep staining of the injected ventricles and the absence of pus when pus was widely distributed throughout the cerebral and spinal subarachnoid spaces, indicating some degree of local

TABLE 10.—*Gentian Violet in the Treatment of Streptococcus Meningitis of Rats* *

Route of Administration	Dose per Kilogram, Gm.	First Dose after Infection	Number of Subsequent Daily Doses	Survival, Days
Intravenously	0.005	4 hours later	2	4†
Intravenously	0.005	4 hours later	2	4†
Subdurally	0.0001	4 hours later	2	4†
Subdurally	0.0001	4 hours later	1	3†
Untreated control	—	—	—	4†
Untreated control	—	—	—	3†

* Infected by subdural injection of 0.1 cc. of 1:15,000,000 dilution of twenty-four hour hormone broth culture.
† Showed streptococci in cultures of heart blood.

TABLE 11.—*Gentian Violet in the Treatment of Streptococcus Meningitis in Dogs* *

Route of Administration	Dose per Kilogram, Gm.	First Dose after Infection	Number of Subsequent Daily Doses	Survival, Days
Intravenously	0.005	24 hours later	4	6†
Intravenously	0.005	24 hours later	3	4†
Intracisternally	0.0001	24 hours later	3	4†
Intracisternally	0.0001	24 hours later	3	5†
Untreated control	—	—	—	5†
Untreated control	—	—	—	6†

* Infected by the intracisternal injection of 0.1 cc. of 1:5 dilution of twenty-four hour hormone broth culture.
† Cultures of heart blood sterile.

TABLE 12.—*Gentian Violet in the Treatment of Experimental Streptococcus Meningitis of Dogs* *

Route of Administration	Dose per Kg., Gm.	First Dose after Infection	Subsequent Daily Doses	Survival, Days	Necropsy
Intraventricularly	0.0003	24 hours; no symptoms	2	4	Ventricles clear; cerebral and spinal
Intraventricularly	0.0003	24 hours; no symptoms	2	3	Ventricles clear; cerebral and spinal
Intraventricularly	0.0004	4 days; symptoms	2	6	Ventricles clear; cerebral and spinal
Intraventricularly	0.0004	4 days; symptoms	1	5	Ventricles pus; cerebral and spinal
Untreated control	—	—	—	5	Ventricles pus; cerebral and spinal

* Infected by the intracisternal injection of 0.1 cc. of 1:5 dilution of twenty-four hour hormone broth culture.

bactericidal and beneficial effect. The results of two experiments of this kind are shown in tables 11 and 12 as examples of the series.

Additional animals were treated with antistreptococcus serum and gentian violet, but with negative results. In these experiments, treatment was not started until about the fourth day after infection when the early symptoms of meningitis were present. In some animals we injected

intraventricularly 0.4 cc. of serum and 0.0002 Gm. of gentian violet per kilogram of weight under ether anesthesia; other animals received approximately the same doses of both serum and dye intraventricularly, along with the immediate injection of serum intravenously or intramuscularly in dose of 2 cc. per kilogram of weight. The results of one experiment of combination therapy of this kind are shown in table 13, and is representative of the series. As a general rule, the results were negative so far as mortality was concerned, although the lives of a few dogs were apparently prolonged by a day or two beyond the untreated controls.

Gentian Violet in the Treatment of Experimental Pneumococcus Meningitis of Dogs.—With these results before us, even less hope was entertained for the curative activity of gentian violet in experimental pneumococcus meningitis. Dogs were infected under ether anesthesia

TABLE 13.—*Antistreptococcus Serum and Gentian Violet in the Treatment of Experimental Streptococcus Meningitis of Dogs* *

Treatment per Kg.	First Treatment after Infection	Subsequent Daily Treatments	Survival, Days	Necropsy
0.4 cc. serum intraventricularly 0.0002 Gm. gentian violet intraventricularly	5 days; symptoms	1	7	Ventriculitis; meningitis
0.4 cc. serum intraventricularly 0.0002 Gm. gentian violet intraventricularly	5 days; symptoms	2	8	Ventriculitis; meningitis
0.4 cc. serum intraventricularly 0.0002 Gm. gentian violet intraventricularly 2 cc. serum intravenously	5 days; symptoms	1	7	Ventriculitis; meningitis
0.4 cc. serum intraventricularly 0.0002 Gm. gentian violet intraventricularly 2 cc. serum intramuscularly	5 days; symptoms	1	7	Ventriculitis; meningitis
Untreated control.....	—	—	6	Ventriculitis; meningitis
Untreated control.....	—	—	7	Ventriculitis; meningitis

* Infected by intracisternal injection of 0.1 cc. of 1:5 dilution of twenty-four hour hormone broth culture per kilogram.

by intracisternal injections of type I pneumococci, and treatment was begun about twenty-four hours later, since symptoms were usually apparent. Repeated intravenous injections of gentian violet in dose of 0.005 Gm. per kilogram were ineffective, and intracisternal injections of 0.0002 Gm. per kilogram under ether anesthesia were likewise without appreciable influence, as shown in the results of one experiment summarized in table 14.

Acriflavine in the Treatment of Experimental Streptococcus Meningitis of Dogs.—Neutral acriflavine by intravenous, intracisternal and intraventricular administration has likewise proved ineffective in our experience in the treatment of experimental streptococcus and pneumococcus meningitis of dogs. The results of one experiment with streptococcus infections is shown in table 15, in which intraventricular injections of doses varying from 0.0003 to 0.0004 Gm. per kilogram were without

result so far as the mortality and duration of life were concerned. It is true, however, that we sometime observed much less pus in the injected ventricle than elsewhere in the subarachnoid space, indicating some degree of local bactericidal effect.

But intravenous injections of 0.005 Gm. and intracisternal injections of 0.0001 to 0.0002 Gm. per kilogram were without effect in both streptococcus and pneumococcus infections, the results of one experiment with the former being shown in table 16.

TABLE 14.—*Gentian Violet in the Treatment of Pneumococcus Meningitis of Dogs**

Route of Administration	Dose per Kilogram, Gm.	First Dose after Infection	Number of Subsequent Daily Doses	Survival, Days
Intravenously	0.005	24 hours later	3	6†
Intravenously	0.005	24 hours later	4	6†
Intracisternally	0.0002	24 hours later	2	4†
Intracisternally	0.0002	24 hours later	3	4†
Untreated control	—	—	—	5†
Untreated control	—	—	—	5†

* Infected by intracisternal injection of 0.1 cc. of 1:100 dilution of twenty-four hour hormone broth culture of type I pneumococcus.
† Cultures of heart blood sterile.

TABLE 15.—*Acriflavine in the Treatment of Experimental Streptococcus Meningitis of Dogs**

Route of Administration	Dose per Kg., Gm.	First Dose after Infection	Subsequent Daily Doses	Survival, Days	Necropsy
Intraventricularly	0.0004	24 hours; no symptoms	1	4	Ventricle clear; cerebral and spinal
Intraventricularly	0.0004	24 hours; no symptoms	2	5	Ventricle clear; cerebral and spinal
Intraventricularly	0.0004	4 days; symptoms	2	7	Ventricle clear; cerebral and spinal
Intraventricularly	0.0003	4 days; symptoms	2	6	Ventricle clear; cerebral and spinal
Untreated control	—	—	—	6	Ventricles pus; cerebral and spinal
Untreated control	—	—	—	5	Ventricles pus; cerebral and spinal

* Infected by the intracisternal injection of 0.1 cc. of 1:5 dilution of twenty-four hour hormone broth culture.

Rivanol in the Treatment of Experimental Streptococcus Meningitis of Dogs.—Negative results were also observed with rivanol in the treatment of streptococcus meningitis of dogs. Treatment with this compound was usually begun about three days after infection by intracisternal injection of the virulent strain of hemolytic streptococcus, but the only encouraging results were observed among dogs treated daily by saline lavage from one of the ventricles to the cisterna magna, followed by intraventricular and intracisternal injections of the drug. But we believe that these results were largely due to the lavage. Certainly the daily intravenous injection of rivanol in dosage of 0.005 Gm. per

kilogram has been without appreciable effect, as likewise the intracisternal and intraventricular injection of 0.0002 to 0.001 Gm. per kilogram, as shown by the results of one experiment summarized in table 17.

Therefore, none of the three dyes compounds employed in our investigation has proved efficacious in the treatment of acute septic meningitis of the lower animals. It is possible, and indeed probable, that better results may have been observed with milder infections, in view of the fact that all of ours were very acute and fulminating infec-

TABLE 16.—*Acriflavine in the Treatment of Experimental Streptococcus Meningitis of Dogs* *

Route of Administration	Dose per Kilogram, Gm.	First Dose after Infection	Number of Subsequent Daily Doses	Survival, Days
Intravenously	0.005	24 hours later	3	5†
Intravenously	0.005	24 hours later	2	4†
Intracisternally	0.0001	24 hours later	3	6†
Intracisternally	0.0001	24 hoursl ater	3	5†
Untreated control	—	—	—	6†
Untreated control	—	—	—	5†

* Infected by the intracisternal injection of 0.1 cc. of 1:5 dilution of twenty-four hour hormone broth culture.
† Cultures of heart blood sterile.

TABLE 17.—*Rivanol in the Treatment of Experimental Streptococcus Meningitis of Dogs* *

Route of Administration	Dose per Kg., Gm.	First Dose after Infection	Subsequent Daily Doses	Survival, Days	Necropsy
Intravenously	0.005	4 days; symptoms	2	6	Ventricles pus; cerebral and spinal
Intraspinally	0.0005	4 days; symptoms	2	5	Ventricles pus; cerebral and spinal
Intracisternally	0.0005	4 days; symptoms	2	6	Ventricles pus; cerebral and spinal
Lavage, intraventricularly, intracisternally	0.0005	4 days; symptoms	2	Lived indefinitely	
Untreated control	—	—	—	5	Ventricles pus; cerebral and spinal

* Infected by the intracisternal injection of 0.1 cc. of 1:3 dilution of twenty-four hour hormone broth culture.

tions with severe suppurative leptomeningitis, but to have done otherwise may have resulted in so many spontaneous recoveries as to render the proper evaluation of results impossible.

Probably one of the most important reasons for failure is the reduced bactericidal activity of these compounds in the presence of pus, and the difficulty of diffusion in the subarachnoid space, but these factors have been already discussed.

SUMMARY

1. By injection into the cisterna magna of normal rabbits, the maximum single tolerated dose of gentian violet (Coleman and Bell)

was found to be from 0.001 to 0.003 Gm. per kilogram. The dose of neutral acriflavine (National) was 0.002 to 0.003 Gm. and rivanol (Hoechst) about 0.0005 to 0.001 Gm. per kilogram, by the same route of injection. The tolerance of dogs with acute streptococcus and pneumococcus meningitis, however, was somewhat less and by repeated intraspinal, intracisternal and intraventricular injection, the usual tolerated dose of the three compounds was from 0.0001 to 0.0003 Gm. per kilogram. These amounts correspond to 0.006 to 0.018 Gm., or 6 to 18 cc. of 1 : 1,000 solutions per 60 kilograms of weight.

2. The bactericidal activity of gentian violet, acriflavine and rivanol for streptococci and pneumococci in purulent spinal fluids varied from a final dilution of about 1 : 1,800 to 1 : 4,000 in an exposure of five minutes at 37 C.

3. Gentian violet, neutral acriflavine and rivanol, by intravenous administration in dose of 0.005 Gm. per kilogram, showed no beneficial effects on the course of experimental staphylococcus, streptococcus and pneumococcus meningitis.

4. Gentian violet, neutral acriflavine and rivanol by intracisternal and intraventricular injection in doses varying from 0.0001 to 0.0004 Gm. per kilogram, had no appreciable effect on the course and mortality of acute experimental streptococcus and pneumococcus meningitis of dogs.

V. IMMUNE SERUMS, ANTIBODY SOLUTION AND LAVAGE IN THE TREATMENT OF PNEUMOCOCCUS AND STREPTOCOCCUS MENINGITIS

WITH THE ASSISTANCE OF
ANNA M. RULE AND BERNARD MADDEN

The intraspinal injection of antistreptococcus serum has been the most commonly employed method of treatment of streptococcus meningitis. Likewise, in the treatment of pneumococcus meningitis, intraspinal injections of antipneumococcus serum have been usually employed. As a rule, these antiserums have also been administered by intramuscular or intravenous injection at the same time. But very little success has attended the serum therapy of these two forms of septic meningitis. Weaver [24] has recorded the recovery of a patient with *Streptococcus viridans* meningitis ascribed to treatment with intraspinal and intramuscular injections of a polyvalent antistreptococcus serum, but such an outcome is certainly an unusual result. During the past six years, I have treated seven cases of streptococcus meningitis with polyvalent antistreptococcus serum by intraspinal and intravenous injection with no recoveries; all of these, however, were of otitic origin, whereas Dr. Weaver's patient had no such primary focus of infection.

24. Weaver, G. H.: A Case of Acute Streptococcus Meningitis with Recovery, J. A. M. A. **72**:1362 (May 10) 1919.

The treatment of pneumococcus meningitis with antipneumococcus serum has likewise been disppointing in my experience, and especially those of otitic or nasal origin. It is true, however, that the prognosis is much better in those cases of meningitis developing during pneumococcus pneumonia, which are sometimes not true meningitis but rather instances of acute meningeal congestion or the so-called "serous meningitis;" the same is true of those occasional instances in which pneumococci are found in cultures of clear fluid without leukocytic exudations. In acute suppurative pneumococcus leptomeningitis of otitic or nasal origin, the prognosis usually is extremely bad and the mortality in general has been reported in the neighborhood of 93 per cent. During the past seven years, I have treated sixteen cases of otitic pneumococcus meningitis with intraspinal and intravenous injections of polyvalent antipneumococcus serum with no recoveries. In four of these the intraspinal injections were of mixtures of antiserum, sodium oleate and boric acid, since Lamar [25] reported mixtures of this kind curative in the treatment of experimental pneumococcus meningitis of monkeys. These did not prove effective in my cases, and Idzumi and I [26] also observed that they have not proved more effective than the serum alone in the treatment of experimental pneumococcus meningitis of rabbits. Litchfield,[27] however, has reported five recoveries in a series of ten cases of meningitis occurring in lobar pneumonia, ascribed to the intraspinal and intravenous injections of Kyes chicken antipneumococcus serum, but to the best of my knowledge the serum has not been reported on in the treatment of acute suppurative meningitis of otitic or nasal origin. In passing, it may be stated that I have employed fresh sterile normal chicken serum by intraspinal injection in doses of 8 to 10 cc. in the treatment of two cases without beneficial effects. Horn [28] has reported the recovery of a mild case of alleged pneumococcus meningitis occurring in a syphilitic patient and treated with intraspinal injections of the patient's own serum, but I am quite sure that autoserum therapy would not prove effective in the treatment of acute cases of otitic or nasal origin.

A far more promising biologic product for the treatment of pneumococcus meningitis is pneumococcus antibody solution. To the best of my knowledge it was first employed by Wieder [29] by intraspinal injection, and his patients rapidly improved only to succumb later to an unsuspected abscess of one of the frontal lobes of the cerebrum. I might

25. Lamar: Footnote 9.
26. Idzumi, G., and Kolmer, J. A.: Footnote 4.
27. Litchfield, Lawrence: Pneumococcus Meningitis, J. A. M. A. **72**:1345 (May 10) 1919.
28. Horn, Will S.: Autoserum Treatment of Pneumococcus Meningitis Complicated by Syphilis, J. A. M. A. **80**:1124 (April 21) 1923.
29. Wieder, H. S.: Footnote 10.

refer here again to my similar experience with a case of acute suppurative pneumococcus meningitis of otitic origin, in which the intraspinal and intramuscular injections of antibody solution were so effective that the patient, a boy, aged 10 years, was up and about, but succumbed suddenly about four weeks later with an abscess of the cerebellum. I believe, then, that antipneumococcus antibody solution is the most promising biologic product available at present for the treatment of pneumococcus meningitis, and somewhat encouraging results have been observed with it in the present investigation devoted to the treatment of experimental infections of dogs.

But I believe that lavage of the ventricles and subarachnoid space in general is by all odds the most valuable means of treatment, and especially when drainage from the cisterna magna is provided. Dandy [30] has recorded the recovery of three cases of septic meningitis in a series of four, ascribed to provision for continuous drainage from the cisterna magna. Two of these were streptococcus infections and one a *Staphylococcus aureus* meningitis; the fatal case was caused by a hemolytic streptococcus. Hill [31] has also advised the institution of continuous drainage by laminectomy.

In the present series of investigations, we have found lavage of the ventricles to the cisterna magna the most efficient of all methods used by us in the treatment of experimental pneumococcus and streptococcus meningitis of dogs. Our studies are being continued along the lines of establishing continuous drainage from the cisterna magna and spinal meninges, combined in some instances with lavage by way of the ventricles and subdurally by means of trephining. The results will be reported later.

Antistreptococcus Serum in the Treatment of Streptococcus Meningitis of Dogs.—Through the kindness of the H. K. Mulford Company an ample supply of stock polyvalent antistreptococcus serum was placed at our disposal for these experiments. Our particular interest was commanded by a lot of concentrated serum furnished by Dr. F. M. Huntoon, because the serum treatment of meningitis particularly demands the use of concentrated products, since there is a limitation to the amounts of serum that may be safely injected at one time into the ventricles, cisterna magna and spinal subarachnoid space.

Dogs were infected in the usual manner under ether anesthesia by intracisternal injections of 0.1 cc. of 1:5 dilution of twenty-four hour brain-hormone broth cultures, and treatment was begun twenty-four hours later before symptoms had developed, or about four days later when signs of meningitis with cloudy spinal fluids were present.

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30. Dandy, W. E.: Footnote 13.
31. Hill, Roland: Footnote 12.

Under anesthesia, serum was injected intraventricularly and intracisternally in dose of 0.2 to 0.3 cc. per kilogram of body weight, but in no instance were beneficial effects observed, the results of one experiment being summarized in table 18.

We have also treated dogs with the serum intraventricularly and intracisternally, combined with intravenous and intramuscular injections of 2 cc. per kilogram without being able to improve the results.

Dogs have also been given the serum intravenously or intramuscularly in dose of 2 cc. per kilogram, along with mercurochrome intra-

TABLE 18.—*Antistreptococcus Serum in the Treatment of Experimental Streptococcus Meningitis of Dogs* *

Route of Administration	Dose per Kg., Gm.	First Dose after Infection	Subsequent Daily Doses	Survival, Days	Necropsy
Intraventricularly	0.2	24 hours; no symptoms	2	5	Severe meningitis
Intraventricularly	0.3	24 hours; no symptoms	1	3	Severe meningitis
Intraventricularly	0.2	72 hours; symptoms	2	4	Severe meningitis
Intracisternally	0.2	24 hours; no symptoms	2	4	Severe meningitis
Untreated control	—	—	—	5	Severe meningitis

* Infected by the intracisternal injection of 0.1 cc. of 1:5 dilution of twenty-four hour hormone broth culture.

TABLE 19.—*Antistreptococcus Serum, Gentian Violet and Mercurochrome in the Treatment of Experimental Streptococcus Meningitis of Dogs* *

Treatment per Kg.	First Treatment after Infection	Subsequent Daily Treatments	Survival, Days	Necropsy
0.0002 Gm. gentian violet intraventricularly 0.005 Gm. mercurochrome intravenously	4 days; symptoms	1	5	Ventriculitis; meningitis
0.0002 Gm. gentian violet intraventricularly 0.005 Gm. mercurochrome intravenously 2 cc. serum intravenously	4 days; symptoms	1	6	Ventriculitis; meningitis
0.0002 Gm. gentian violet intraventricularly 0.005 Gm. mercurochrome intravenously 2 cc. serum intramuscularly	4 days; symptoms	2	6	Ventriculitis; meningitis
Untreated control.....	—	—	5	Ventriculitis; meningitis

* Infected by intracisternal injection of 0.1 cc. of 1:5 dilution of twenty-four hour hormone broth culture per kilogram.

venously in dose of 0.005 Gm. per kilogram and gentian violet in dose of 0.0002 Gm. per kilogram by intraventricular injection, but without appreciable effects, the results of one experiment of this kind being summarized in table 19.

But when one of the ventricles was first washed through to the cisterna magna by the injection of about 6 cc. of warm saline solution per kilogram of weight, followed by the intraventricular injection of serum, cures were effected. In conducting these experiments under ether anesthesia, a trephine was first made with the introduction of a

needle into one of the lateral ventricles; then a needle was inserted into the cisterna magna, followed by drainage of purulent fluid and the slow intraventricular injection of warm saline solution. Each dog of approximately 5 to 10 Kg. weight was given between 25 and 40 cc. of saline in this manner, and the treatment was concluded by injecting 0.2 to 0.3 cc. of serum per kilogram into the ventricle and sometimes into the cisterna magna. The results of an experiment of this kind are summarized in table 20.

TABLE 20.—*Lavage and Antistreptococcus Serum (Concentrated) in the Treatment of Experimental Streptococcus Meningitis of Dogs* *

Treatment per Kg.	First Treatment after Infection	Subsequent Daily Treatments	Survival, Days	Necropsy
6 cc. saline lavage right ventricle..... 0.3 cc. serum into both ventricles 2.0 cc. serum intravenously	4 days; symptoms	1	Indefinitely	0
6 cc. saline lavage right ventricle..... 0.3 cc. serum into both ventricles 2.0 cc. serum intravenously	4 days; symptoms	1	Indefinitely	0
6 cc. saline lavage right ventricle.....	4 days; symptoms	1	Indefinitely	0
Untreated control.....	—	—	5	Ventriculitis; meningitis
Untreated control.....	—	—	7	Ventriculitis; meningitis

* Infected by intracisternal injection of 0.1 cc. of 1:5 dilution of twenty-four hour hormone broth culture.

Lavage in the Treatment of Experimental Streptococcus and Pneumococcus Meningitis.—We believe the larger part of the success attending these experiments is to be credited to the lavage, since lavage alone has yielded equally good results, as shown not only in table 20 but also in table 22. Lavage alone with warm saline solution from the ventricles to the cisterna magna has resulted in saving a number of dogs infected with our strain of hemolytic streptococcus and type I pneumococcus, when all of the untreated controls have perished in the usual time of four to seven days after infection by intracisternal inoculation. In some instances, lavage of one ventricle has been sufficient, but recoveries have followed lavage of either one or both although the latter has been a slightly severer treatment by reason of trephining both sides of the head.

Probably lavage from the cisterna magna to the lumbar region of the spinal subarachnoid space is helpful, but we have not found this necessary in the treatment of these experimental infections of dogs. We have reason to believe that the institution of continuous drainage from the cisterna magna or lumbar subarachnoid space will still further improve the results, and furnish a method of value in the treatment of septic meningitis of human beings.

Antipneumococcus Serum and Antibody Solution in the Treatment of Experimental Pneumococcus Meningitis of Dogs.—As previously

mentioned, Idzumi and I have not been able to influence appreciably the course and mortality of experimental pneumococcus meningitis of rabbits with either type I antipneumococcus serum alone, or in combination with sodium oleate and boric acid. Similar negative results have been observed in the present investigation employing dogs infected with intracisternal injections of type I pneumococcus and treated with homologous antiserum administered intravenously, intraventricularly and intracisternally. In one experiment we also employed intracisternal injections of diluted ox bile alone and in combination with the serum, but with negative results.

TABLE 21.—*Antibody Solution (Huntoon) in the Treatment of Experimental Pneumococcus Meningitis of Dogs**

Treatment per Kg.	First Treatment after Infection	Subsequent Daily Treatments	Survival, Days	Necropsy
0.4 cc. intraventricularly..... 0.4 cc. intravenously	36 hours; symptoms	2	6	Purulent ventriculitis; purulent meningitis
0.4 cc. intraventricularly..... 0.4 cc. intravenously	36 hours; symptoms	2	5	Purulent ventriculitis; purulent meningitis
0.4 cc. intraventricularly..... 0.4 cc. intravenously	36 hours; symptoms	2	7	Ventricles clear; purulent meningitis
Untreated control.....	—	—	5	Purulent ventriculitis; purulent meningitis

* Infected by the intracisternal injection of 0.1 cc. of 1:60 dilution of a twenty-four hour broth culture of type I pneumococcus per kilogram.

Antibody solution, however, appeared to yield a somewhat better result, although as yet we have not succeeded in saving a single animal with it alone. As shown in table 21, the intraventricular injection of 0.4 cc. per kilogram, along with intravenous injections, sometimes prolonged lives by a day or two, but when given after lavage with saline solution, the majority of animals survived and lived indefinitely. It is probable, however, that these results were due in larger part to the lavage, but antibody solution can be injected safely into the ventricles and subarachnoid space and may aid in curing pneumococcus infections. This is likely to be especially true of concentrated antibody solution which we used in one experiment.

It would appear that antistreptococcus and antipneumococcus serums are unable to effect the cure of severe septic meningitis. This is certainly true of ordinary methods of administration by intraspinal and intravenous injection, as indicated not only by experiments but especially by clinical experience. Huntoon's antipneumococcus antibody solution holds out somewhat more hope for success, but we believe at present that it will likewise fail if used alone in the treatment of the severe infections of otitic or nasal origin. But lavage of the subarachnoid space, preliminary to the intraventricular or intracisternal injection of antibody solution, bids fair to prove an efficient means for the treatment of pneumococcus meningitis.

SUMMARY

1. Polyvalent antistreptococcus serum administered by intramuscular, intravenous, intracisternal and intraventricular injection has failed to influence appreciably the cause and mortality of experimental hemolytic streptococcus meningitis of dogs.

2. Type I antipneumococcus serum administered by intramuscular, intravenous, intracisternal and intraventricular injection has failed to influence appreciably the course and mortality of experimental type I pneumococcus meningitis of dogs.

3. The intravenous, intraventricular and intracisternal injection of antipneumococcus antibody solution has exerted a slight degree of curative activity in the treatment of pneumococcus meningitis.

4. Lavage of one or both of the lateral ventricles to the cisterna magna has proved effective in the treatment of severe experimental streptococcus and pneumococcus meningitis of dogs. This may be combined with the administration of antibody solution by subthecal injection in the treatment of pneumococcus meningitis, or by the injection of gentian violet in the treatment of streptococcus meningitis.

TABLE 22.—*Lavage and Concentrated Antibody Solution in the Treatment of Experimental Pneumococcus Meningitis of Dogs**

Treatment per Kg.	First Treatment after Infection	Subsequent Daily Treatments	Survival, Days	Necropsy
8 cc. lavage right ventricle..... 0.3 cc. antibody both ventricles and cistern 2.0 cc. antibody subcutaneously	36 hours; symptoms	1	Lived indefinitely	0
8 cc. lavage right ventricle..... 0.3 cc. antibody both ventricles and cistern 2.0 cc. antibody subcutaneously	36 hours; symptoms	1	Lived indefinitely	0
8 cc. lavage right ventricle..... 0.3 cc. antibody both ventricles and cistern 2.0 cc. antibody subcutaneously	36 hours; symptoms	1	Lived indefinitely	0
8 cc. lavage right ventricle..... 0.3 cc. antibody both ventricles and cistern 2.0 cc. antibody subcutaneously	36 hours; symptoms	1	Lived indefinitely	0
10 cc. lavage right ventricle to cistern....	36 hours; symptoms	1	Lived indefinitely	0
10 cc. lavage right ventricle to cistern....	36 hours; symptoms	1	Lived indefinitely	0
Untreated control.....	—	—	2	Ventriculitis; meningitis
Untreated control.....	—	—	3	Ventriculitis; meningitis
Untreated control.....	—	—	3	Ventriculitis; meningitis
Untreated control.....	—	—	3	Ventriculitis; meningitis

* Dogs infected by the intracisternal injection of 0.1 cc. of brain-hormone broth culture of type I pneumococcus per kilogram of weight.

SOME PHASES OF STREPTOCOCCIC INFECTION IN ACUTE MASTOIDITIS*

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For a number of years I held to the impression that the type of infection in acute mastoiditis had very little to do with the clinical symptoms, and that no matter what organism predominated, the course of the condition was not materially altered by the character of the infection. Latterly, I have become convinced that the predominating type of infection does play a very important rôle, and that, furthermore, epidemic types of infection causing mastoiditis are the most virulent in their activity. And yet, on the other hand, in the majority of the cases in which I have found the most extensive mastoid necrosis, there has been a mixed infection, with the so-called less harmful bacteria predominating. This doubtless is due to the fact that, in a given series of cases, as, for instance, two years ago, when during the winter months I operated on more than sixty patients with acute mastoiditis, a large proportion will be charity patients in hospital services, in whom there has been delay in seeking attention, and delayed cases always, in my experience, show a mixed infection. On the other hand, when we have epidemics of respiratory congestive diseases, such as that which prevailed the past fall and winter practically all over the country, called influenza for lack of a better name, the pathogenic bacillus is likely to prove of the streptococcic type, and when this is hemolytic, the development of the mastoiditis is usually rapid and quickly destructive, with, in most cases, rapidly developing infection of the blood stream. Furthermore, mastoiditis in these cases is quite likely to be monobacillary.

Referring again to my series of cases two years ago, I may say that in sixty of the patients less than one-fifth showed the hemolytic type of streptococcus in the cultures grown from pus obtained from the mastoid wound, whereas in eight mastoidectomies, seven of which were performed on children over a period of three weeks this last winter (all private patients), the hemolytic type of streptococcus was found in every case by culture from the mastoid wound, and several showed similar infection on blood culture.

As a basis for this paper, I am taking the histories of three cases as the subject for analytic study and comment. Most of my conclusions will be derived from the last case, so the first two cases will be rather briefly considered.

* Read by invitation before the Section on Otology and Laryngology of the College of Physicians, Philadelphia, March 17, 1926.

REPORT OF CASES

CASE 1.—A boy, white, aged 8 years, was admitted to the hospital with a temperature of 101.5 F., pulse 90, complaining of pain in the right ear and tenderness over the mastoid region, with sudden onset, following an acute attack of inflammation of the middle ear, which began three days before his admission. The diagnosis was acute mastoiditis.

History.—About two years before this, the child underwent an operation for mastoiditis on this side, but since that time, up to his admittance to the hospital, he had no trouble with this ear.

Laboratory Examination.—This was made before the operation. Urinalysis showed occasional pus cells and a few bacteria, otherwise it was negative; blood, total white count, 24,000; polymorphonuclears, 83; lymphocytes, 15; large mononuclears, 2.

Operation.—The mastoid was opened and was found to contain a small amount of thin, seropus, and a large quantity of granulations, but no bone involvement. Evidence of new bone formation was found on the inner plate. An iodoform drain was inserted and the incision was closed with chromic catgut. The operation lasted seventeen minutes, and nitrous oxide gas anesthesia was used.

A culture taken from the mastoid reported streptococcus of the hemolytic type in pure culture.

The patient reacted normally to the operation, and the next day was feeling well, and complained only of slight tenderness around the operative field. The dressing was changed, and a moderate amount of discharge was found.

On the third day, the stitches were removed, the drain having been taken out on the day after operation. The patient developed an irregular temperature, of a remittent type, which decreased slightly each day.

Four days after operation, the boy was discharged from the hospital in a satisfactory condition. The wound continued to discharge for about two weeks following, but gradually cleared up in normal time.

Comment.—This case calls for little comment, other than to dwell on the great rapidity with which it developed, the intense blood stream infection in so short a time, and the almost immediate breaking down of the old scar tissue by a pure hemolytic type of streptococcus growth. Before dismissing this case from consideration, I should like to call attention to a laboratory finding which is not without significance, that is, that it was with the greatest difficulty the culture was kept alive, showing that the child's resistance was strong, and that his own phage was overcoming the virulent infection at this time. Doubtless had I waited two or three days before operating, this resistance would have been broken down, with a resulting prolonged recovery, or perhaps fatality.

The next case is noteworthy chiefly as an example of the rapidly destructive action of the hemolytic type of streptococcus, but has some clinical features which may justify its being reported in detail.

CASE 2.—A boy, white, aged 8 years, was convalescing from a severe attack of scarlet fever, and was admitted to the hospital complaining of pain in the left ear and fever. The patient gave a history of acute purulent otitis media of two weeks' duration. Five days before admission to the hospital, mastoid tenderness developed. He continued to have an irregular temperature of 101 to 102 F., and complained of headache and general malaise. Three days before admission

to the hospital, the drum membrane was opened, though it was not bulging, and but slightly inflamed. The diagnosis was acute mastoiditis.

Laboratory Examination.—Blood count, 24,150 white cells; large mononuclears, 1; small lymphocytes, 4; polymorphonuclears, 85. Urinalysis: albumin, trace; pus cells, a few; a few hyaline and epithelial casts. A roentgenogram showed cloudiness of all cells of the mastoid.

Operation.—The entire mastoid process was found to be riddled with pus and granulations; no dura was exposed. The operation lasted seventeen minutes, and nitrous oxide anesthesia was used.

The child made an uneventful recovery from the operation. A culture from the mastoid was reported positive for hemolytic type of streptococcus. A culture of the blood taken three days after operation was reported negative. Following operation, the temperature dropped from 104.2 to 100 F., where it remained until the next day at noon, when it again rose to 104.2 F. Two days after the operation the temperature rose to 101, and dropped down to normal that evening. The next day it returned to 101, and then dropped to normal; the next day it rose to 100 F., and on the eighth day following operation, the temperature returned to normal, where it remained.

The patient left the hospital a week following operation. His ear was healing rapidly, and there was only a slight amount of thin, seropurulent discharge. He was free from fever, but began to complain of pains in his right ear.

After remaining at home for three days, the child was readmitted to the hospital, complaining of pain, with a temperature of 100 and a pulse rate of 100, and there was swelling behind the right ear. This was the ear he complained of before leaving the hospital, and on which a simple mastoidectomy had been performed four years before.

Laboratory Examination.—Blood: 18,250 white cells; small lymphocytes, 12; large monomuclears, 5; polymorphonuclears, 83. Urinalysis showed albumin, 2 plus; the blood showed pus and hyaline casts.

Operation.—This was performed with nitrous oxide anesthesia. The mastoid was cleaned out, and a large amount of granulations, some pus, and a few small areas of necrotic bone were found. The operation lasted twenty minutes.

The patient made an uneventful recovery. The temperature was irregular; following operation it dropped from 101.2 down to 98 F., and continued with fluctuations, not exceeding 100 degrees, until the last three days the patient was in the hospital. On those days the temperature went up a little higher, but was not accompanied by any alarming symptoms.

The dressing was changed on the third day, and a thin, seropurulent discharge of moderate amount was found. On the left side there had developed a rather profuse, thick, white discharge, which necessitated the insertion of a small drain. This discharge subsided in a few days. The side which was last operated on healed rapidly. There was only slight inflammation around the incision. The discharge grew rapidly less in amount.

The patient improved rapidly, and was discharged from the hospital eleven days following operation. Both ears became normal.

Comment.—It is remarkable in this, as in the previous case, how quickly the destruction of well-organized scar tissue came about in an old mastoid wound. Except for the absence of bone, the appearance was that of a mastoid abscess of long standing.

The last case is one so full of interesting clinical and laboratory phases that I feel it would almost justify this paper.

Case 3.—A girl, white, aged 7 years, was admitted to the hospital with a temperature of 106 F., and a pulse rate of 150, complaining of chilly sensations and pain in the right ear.

History.—The child had been sick for about a week, apparently with influenza, during which time she had a slight earache on the right side, which grew progressively worse. During her illness the temperature had been very irregular, sometimes remitting nearly to normal, then became high again. Two days before she was admitted to the hospital, the ear began discharging slightly. There was tenderness over the cardinal points of the mastoid. The diagnosis was acute mastoiditis.

Laboratory Examination.—Urinalysis: a few epithelial cells, 1 to 3 pus cells to the field under high power magnification, and many bacteria. Blood: total white cells, 20,000; small lymphocytes, 5; large mononuclears, 4; polymorphonuclears, 91. A roentgenogram showed a cloudy right mastoid, with increasing density in the region of the antrum. The cell outlines could be made out, but were hazy. The diagnosis was acute right mastoiditis, with possible necrosis of cells.

At the time of operation the temperature was 106 F., the pulse rate 150. When the bone was exposed, it was found to be normal in appearance, and not eroded, but bled very freely when cut. Inside, a moderate amount of seropurulent material was found, from which culture was made. There was a fair amount of cell necrosis, which extended upward toward the angle of the lateral sinus and dura. The tip was but slightly involved. Bone over the sinus was not diseased, but was in good condition, as was the rest of the inner wall. No dura was exposed. An iodoform drain was inserted, and the wound was closed with chromic catgut suture. The operation, performed under nitrous oxide anesthesia, lasted twenty-two minutes.

Following operation, the temperature dropped to 100.4 F., and the patient reacted normally. The next day she appeared to be comfortable, and did not complain, but that morning she had an elevation in temperature to 104.6. The report on blood culture and culture from the mastoid was as follows: "Culture taken from mastoid and blood shows rapidly growing streptococcus of hemolytic type. The character of the organism and of the cultures indicate that the organism is mixed with a bacteriophage. The prognosis under these circumstances is good."

The child appeared pale and washed out, so a transfusion was given that afternoon, 200 cc. of whole blood being taken from the mother. Following the transfusion, the temperature went up to 104.8. Another blood culture was taken, which was reported to be negative.

On the evening of the following day the temperature, which had dropped to normal, rose to 103.8, and was accompanied by a rigor, lasting five minutes. The next morning there was a similar rise in temperature—from 98.8 to 102.4—accompanied by a severe rigor, which lasted about twenty minutes. That afternoon the temperature again rose sharply to 104.8.

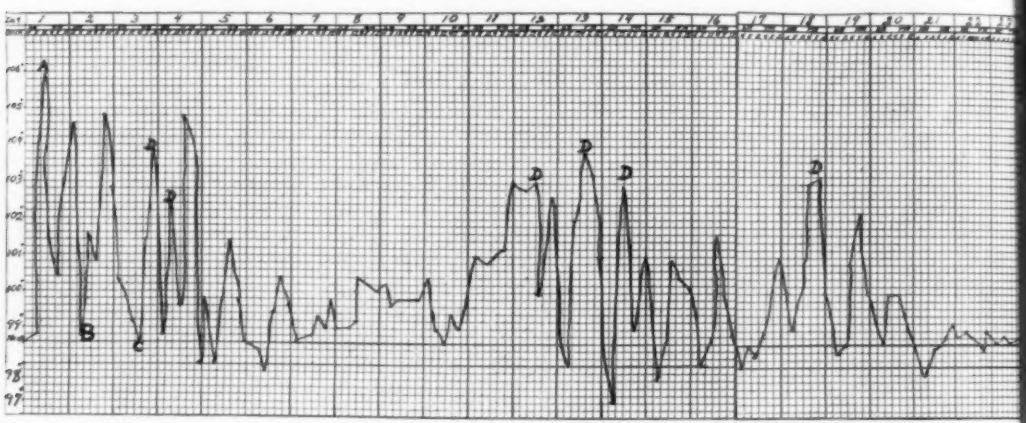
During all this time the patient had never complained of pain or any discomfort. She played with toys and seemed bright and cheerful. Her appetite was very good, and she constantly complained of being hungry. The dressing was changed on the second day following operation, and a small amount of serosanguineous fluid was found. The wound appeared to be in good condition. The patient was watched closely for any swelling in the posterior triangle of the neck, tenderness around that side, pain on motion of the head, headache, etc. None of these was found, and aside from the chills and fever, the patient appeared to be making a normal recovery. Blood count made four days after operation was as follows: Total white cells, 21,350; small lymphocytes, 20; large mononuclears, 7; polymorphonuclears, 73.

From this time until she left the hospital, six days later, the child had no more rigors. The temperature continued to be of the same irregular character, but seemed to become gradually lower. The general condition of the child appeared good.

The day after the patient returned home, she had another rise in temperature to 103.2, and this was accompanied by a severe rigor. Following this, the temperature dropped to 97. The next morning, about the same time, she had

another rigor. A consultation was held. The patient was examined by a neurologic surgeon. He found all reflexes normal, eye-grounds negative, but when lumbar puncture was made he reported fluid under marked pressure, although clear. By the Ayres-Tobey manometric test, he found also that the jugular vein on the operated side was completely blocked, and confirmed a provisional diagnosis of lateral sinus thrombosis. Despite all this, the general condition of the patient appeared to be so good that it was decided to wait a little longer before jugular ligation. The next day, as was expected, the patient had another rigor, which came on about noon.

During all this time, notwithstanding the chills and septic temperature, the patient was steadily improving. She had an enormous appetite, and gained weight rapidly. The wound was closing nicely, and there was very little discharge. There was no abnormal tenderness about the neck or head, nor any limited range of motion. The patient had been free from chills now for three days, but continued to show a daily rise in temperature, which went up to around 101. On the evening of the eighteenth day following operation, her temperature went up



Temperature chart of case 3. A, operation; B, transfusion; C, dressing changed; D, rigor.

to 103.4, and was accompanied by marked rigor. Following this, it again dropped to subnormal. On the following day it went up to 102.2, and there were also rises on each succeeding day for five or six days later, when it finally remained normal.

Although free from fever, the patient was kept quiet for several days, and shortly afterward was discharged, cured, having no complicating sequelae from her sickness, other than a slight lagging of the left foot, which in time completely disappeared.

Comment.—The first question that might be raised probably would be: Why was this patient not operated on for lateral sinus thrombosis? The answer to this is more or less involved. First, I was not convinced that there was a complete jugular block, and as I have in previous instances witnessed a happy termination to conservative treatment in cases in which apparently there was only partial occlusion, I felt justified in not being radical in this instance. I may refer to a rather unusual

case reported by me to the American Laryngological, Rhinological and Otological Society, at its meeting in Atlantic City, in May, 1918.[1] A boy, aged 11 years, had a typical clinical picture of lateral sinus thrombosis for nearly two weeks, and although an operation was performed and the sinus exposed, since there apparently was blood flowing through the sinus and not a complete occlusion, the sinus was not opened and the patient recovered. Second, the blood stream infection seemed to be clearing up, which would indicate that the infection was being cared for by natural agencies. Third, I placed some faith in the hypothesis of the bacteriologist at the Methodist Hospital, Memphis, Mr. L. O. Dutton, who, after a long series of observations, claims to be able to foretell results in streptococcic blood stream infection with 100 per cent of certainty, and who in this case gave a favorable prognosis —in fact, he said the child would recover.

Since this is rather a strong claim, I have briefly summarized the conclusions of Mr. Dutton, as presented in a paper read before the Society of American Bacteriologists at Madison, Wis., in December, 1925.

He recognizes several different types of streptococci, which, he says, exist as mixed strains. They are designated as mixed strains because each is combined with a bacteriophage. The bacterium and the bacteriophage are theoretically a balance with each other—the lytic action of the bacterium, with the defensive action of the bacteriophage. When grown on artificial mediums, this balance is disturbed, and one or the other predominates. Either the bacteriophage overcomes the bacterium, or the bacterium is strengthened and kills the bacteriophage. The bacteriologist arrives at his conclusions by observing the individual morphologic characteristics of the bacterium, and the appearance of the colonies, when grown on a suitable medium.

In patients in whom the blood culture was positive, and in whom the bacteriophage predominated, within from thirty-six to seventy-two hours later Dutton has observed that the blood culture was sterile; and in conditions in which the bacteria were found to predominate, the blood culture remained positive, with a fatal termination.

In the case referred to, the blood culture taken at noon the day of operation was positive for streptococcus of the hemolytic type, and the blood culture taken at the same time on the following day was negative.

Here is another interesting feature of this case. The phage developed in the child's blood was so active that the streptococci, as in the first case reported, could scarcely be kept alive in culture, and the blood in a case

1. McKinney, R.: Laryngoscope **29**:13 (Jan.) 1919; to be published in the Journal of Infectious Diseases.

of mastoiditis with streptococcic blood stream infection, treated with injections of this phage, became negative within twenty-four hours after administration of the phage.

CONCLUSION

I am by no means recording this case as a claim for nonsurgical interference in lateral sinus thrombosis, but realizing that a conservative attitude in this respect seems to have gained ground over a former tendency to ligate immediately the jugular and open the sinus in such cases, I am wondering if we are finally going to arrive at some definite means to guide us in assuming a nonsurgical attitude. Perhaps in these septicemias, bacteriologic methods, such as those mentioned, may have a positive value.

While we know that we have lateral sinus thrombosis when there is no blood-stream infection, a mild leukocytosis and moderate temperature variations, and realize that bacteriology could be of little service in such cases, yet when there is found an active blood stream infection, marked leukocytosis and positive evidence of sepsis, as shown by rigors and violent and extreme temperature fluctuations, then the bacteriologist may come to our aid. Especially may this prove true in cases of acute mastoiditis with streptococcic blood stream infection, and it is in these bacteremias also that whole blood transfusions may prove valuable.

POSTDIPHTHERITIC STENOSIS OF THE LARYNX *

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In this paper, when I speak of diphtheritic stenosis of the larynx, I mean, not acute laryngeal diphtheria in which the O'Dwyer method of intubation has been and should be used, but the chronic type in which it has been necessary to reintubate the patient after a period of a month to six weeks; in other words, chronic tube cases.

John Rogers,[1] in his paper on treatment of chronic obstruction in the larynx and trachea, read before the American Laryngological Association on June 3, 1905, stated: "Hypertrophic subglottic laryngitis is most commonly encountered in retained tube cases, less often in those with a retained tracheal cannula and almost always after diphtheria."

Diphtheria as an etiologic factor in stenosis of the larynx is well established. Coplin [2] in his "Special Pathology," showed in 220 patients examined by Councilman, that the larynx is involved more than any other part of the airway.

Imperatori [3] reported a case of tracheal stenosis following diphtheria, and stated that the diphtheritic erosion and repeated intubation caused the cicatricial stenosis. Tucker [4] mentions the same factor, as well as trauma in attempting intubation, as a possible cause of injury to the arytenoids.

Realizing the pathology of the infection, knowing generally what constant irritation will do, can we not expect the same condition to exist in a larynx by continued use of intubation tubes and by the trauma caused by repeated intubations, performed under rather trying conditions following auto-extubation? We have all seen improvement in carcinoma of the esophagus after gastrostomy, temporary though it be, in tuberculosis as well as in carcinoma of the larynx after tracheotomy; why cannot we expect the same in diphtheria of the larynx?

In order to prevent this condition, is it not better to perform a tracheotomy to put the larynx at rest, not losing sight of the wonderful work of O'Dwyer in the vast number of patients saved by that method?

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* Read before the American Laryngological, Rhinological and Otological Society, Philadelphia, Jan. 23, 1926.

1. Rogers, John: Tr. Am. Laryngol. Sc., 1905.
2. Coplin, M. L.: Special Pathology, Ed. 4, p. 684.
3. Imperatori, Charles J.: Cicatricial Stenosis of the Trachea, Arch. Otolaryng. **1**:624 (June) 1925.
4. Tucker, Gabriel: Laryngostomy for Laryngeal Stenosis, Arch. Otolaryng. **1**:157 (Feb.) 1925.

TRACHEOTOMY

Jackson [5] and Tucker [4] have definitely shown in laryngostomies that less irritation is caused by tubing covered with Penrose tubing than when not covered. This fact has been noticed by me in my cases.

In the twenty-five patients that I have had the good fortune to see in a relatively short space of time, intubation and extubation have been performed on some from 11 to 40 times before resorting to tracheotomy. One patient had been in the hospital for five and one-half years, and another for four years; the vast majority had been in the hospital for almost a year, their ages running from 11 months to 28 years. Two had tracheal stenosis, one had a fibrous band across the arytenoids and four had laryngostomies. On twenty, tracheotomy was performed, and the period of actual treatment of the cases extended over a period of from two to three years.

As the tracheotomy operation is well understood, nothing can be gained by mentioning the method further.

Dr. Pringle, superintendent of the Essex County Isolation Hospital, firmly believes in early tracheotomy in laryngeal diphtheria; that is, if it is impossible for a patient to go without the tube for twenty-one days subsequent to the first intubation. Since I have been performing early tracheotomies and have had the cooperation of Dr. Pringle at that hospital, it has been surprising what quick results have been obtained by putting the larynx at rest, and in a number of patients there has been no need of any further treatment.

It might be said that these patients would have progressed just as well by further intubation with special or oversized tubes, but I firmly believe that less laryngeal trouble will arise following diphtheria if tracheotomies are performed early.

I do not wish for a moment to be understood that I advise tracheotomy in acute diphtheritic stenosis, but I do advise tracheotomy in chronic diphtheritic stenosis after four to six weeks, if the patient cannot be permanently extubated, notwithstanding the statement of Dr. Rogers in the last paragraph of his article, mentioned in the foregoing, in which he states that "Even if an intubation tube should have to be worn permanently, this is far preferable to the alternative of a tracheal cannula."

PROCEDURES

In some cases, laryngeal bouginage has been done after tracheotomy; in others, granulations have been removed, and after all other methods had failed, laryngostomies, the laryngostomies following the method of

5. Jackson, Chevalier: Peroral Endoscopy and Laryngeal Surgery, 1915, p. 628.

Fig. 1.—Tracheal stenosis following diphtheria, before and after treatment, as in cases 16 and 18.

Jackson and Tucker, and the closure of the laryngostomic fissures following closely that of Nassau.

Harry L. Baum [6] of Denver shows a post attachment to keep the upper part of the laryngostomy opening from closing. I think it is a good procedure, and, had I been familiar with it, probably would have used it in two of my patients in whom I had to enlarge the opening, which was done by rubber tubing, similar to the method followed by Iglauer.

All of the patients were under treatment from six months to three years.

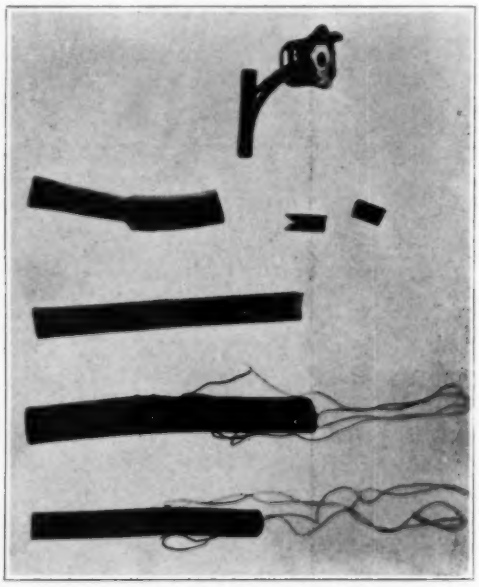

Fig. 2.—Laryngostomy tube and rubber tubing used in cases 2, 3, 4 and 5.

Before any attempt was made to decannulate, infected tonsils were removed. The influence of disease in all laryngeal cases is important, and the diseased tonsils, as well as any nasal infection, should be eradicated before any work is attempted. In the case of J. E. (case 5), the entire wound took on a more healthy appearance after tonsillectomy, and there was considerably less mucus present. This was also noticed in one of Tucker's patients.

Following these various operations, the voice has been good, although somewhat hoarse and rough.

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6. Baum, Harry L.: A New Procedure for Postoperative Care of Laryngostomy, Arch. Otolaryng. **1**:581 (Dec.) 1925.

RESULTS

The net results have been: seventeen patients decannulated and cured; three still under treatment (in one of whom it is necessary to perform a laryngostomy); one patient, a child, aged 2½ years, died of miliary tuberculosis six months after decannulization; another died in convulsions two years after decannulization, but with the fissure not closed (cause of death not known). These two deaths cannot be counted as deaths during treatment. Three other patients died from toxemia, not as a result of tracheotomy, as the case reports show. Altogether, tracheotomy was performed in twenty patients.

Fig. 3.—Roentgenogram, showing laryngostomy tube and rubber tubing in situ in case 2.

REPORT OF CASES

CASE 1.—*Cicatrical Stenosis of the Larynx.*—C. P., aged 8, was admitted to the Essex County Isolation Hospital on Jan. 2, 1917, with diagnosis of laryngeal diphtheria. At this time, a tracheotomy was performed by Dr. Lynah, and the child had been in the hospital five and one-half years prior to my first visit. Apparently very little, if any, laryngeal treatment had been instituted from 1917 to 1922. At regular intervals from 1922, the trachea was dilated and on May 25, 1923, the tonsils were removed prior to decannulization. The patient was decannulated on June 28, 1923, and was permitted to go until May 3, 1924, when a plastic operation, following the technic of Nassau,[7] was performed. The post-

7. Nassau, Charles F.: Closure of Laryngostomic Fistulas, Arch. Otolaryng. **1**:632 (June) 1925.

operative treatment was uneventful, and, at the time of writing, the opening was completely closed. No recurrence of any stenosis has occurred in two years. Result: the child was cured.

Case 2.—*Cicatrical Stenosis of the Larynx with Partial Loss of Epiglottis.*—M. M., a girl, aged 11, was admitted to the Essex County Isolation Hospital on Oct. 11, 1918. On Nov. 26, 1919, to get rid of the intubation tube, tracheotomy was performed by Dr. Lynah. This child had been in the hospital four years prior to my first visit. At various times in 1922, supraglottic granulations were removed by direct laryngoscopy, and the trachea was dilated. No progress was being made under this treatment and on Oct. 5, 1922, a laryngostomy was performed. Subsequent treatment was uneventful until Feb. 6, 1923, when there was a slight perichondritis of the thyroid cartilage on the left side. After the epithelium had completely grown over the larynx, the tonsils were removed on December 13, and after a test period ended, the laryngostomy opening was closed on May 8, 1924. The operation was uneventful other than at the end of three days, due to a panic condition of the patient, it became necessary to insert a no. 1 Jackson tracheotomy tube at the upper angle of the wound. This was immediately corked, and the child made an uneventful recovery. At various

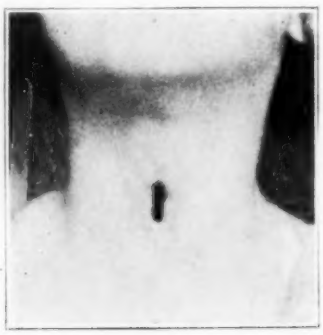

Fig. 4.—Laryngostomy opening prior to plastic closure (after the method of Nassau).

times during the year the trachea was dilated, and on Nov. 18, 1925, the entire tube was removed. At the time of writing there was no recurrence of stenosis.

Case 3.—*Cicatricial Stenosis of the Larynx.*—W. G., a boy, aged 3, was admitted to the Essex County Isolation Hospital in May, 1921. On May 8, 1922, in order to get rid of the intubation tube, a tracheotomy was performed, using a no. 3 Jackson tube. The child had been in the hospital for a year and a half prior to my first visit. At various times supraglottic granulations were removed. No progress was being made by tracheal bouginage, and at the Mountainside Hospital, on Dec. 28, 1922, a laryngostomy was performed. The tube was removed on March 19, 1924. This period was complicated at various times by bronchial pneumonia and in October, 1924, the patient suffered from an attack of parotitis. On June 10, 1925, tonsillectomy was performed, and on November 18 some granulations on the inner surface of the laryngostomic opening were removed. The condition at this time warranted the closure of the laryngostomic opening, but two days later, November 20, in the early morning, I received a telephone call stating that the patient was in a convulsion; the child died before he reached the hospital. The cause of death cannot be accounted for, as there certainly was no stenosis or laryngeal trouble to cause it. Permission for necropsy was not obtained.

CASE 4.—*Cicatricial Stenosis of the Larynx.*—L. F., a girl, aged 2, was admitted to the Essex County Isolation Hospital on Feb. 23, 1922. She had been in the hospital nine months prior to my first visit. After various attempts had been made to dilate by the O'Dwyer method of intubation tubes, it was decided to perform a tracheotomy on June 3, using a no. 2 Jackson tube. Little progress had been made by tracheal bouginage, and on April 23, 1923, laryngostomy was performed. Postoperative treatment was uneventful and the laryngostomy tube was removed on June 2, 1924, after the epithelium had completely covered the larynx. On April 28, 1925, tonsillectomy was performed. At various times, the patient suffered from acute rhinitis, and the closure of the laryngostomic opening has been postponed; at the present time, the patient is going through a test period. Result: The patient was cured but the opening is not yet closed.

CASE 5.—*Cicatricial Stenosis of the Larynx Due to High Tracheotomy.*—J. E., a boy, aged 14, was admitted to St. Michael's Hospital on Oct. 15, 1923, with the history of having had diphtheria five years previously, at which time an emergency

Fig 5.—Photograph taken after plastic closure in case 2 (seen in fig. 4).

tracheotomy had been performed. From that time until he came under my care, very little, if any, tracheal treatment had been instituted. On October 23, an attempt was made to perform a low tracheotomy, but there was quite an island of cartilage intervening and two weeks later a laryngostomy was performed. The larynx was gradually dilated, and covered with epithelium, and on April 8, 1925, the laryngostomy tube was removed. On April 29, his tonsils, which were infected, were removed. Prior to tonsillectomy there was an excessive amount of mucus flowing from the tracheal opening; this ceased immediately after the tonsillectomy. From April 29 until Dec. 10, 1925, nothing eventful took place, and on that date the laryngostomic opening was closed, following the procedure of Nassau. At the time of writing the wound was healed and the patient was discharged. Result: Cured.

CASE 6.—*Hypertrophic Stenosis of the Larynx.*—J. L., a boy, aged 6, was seen at the Essex County Isolation Hospital on March 16, 1922. The condition of this patient cleared up after tracheal bouginage, the trachea being dilated up to no. 27 with Jackson's tracheal dilator. Result: Cured.

CASE 7.—*Hypertrophic Stenosis of the Larynx.*—H. S., a girl, aged 6, was seen at the Essex County Isolation Hospital on March 16, 1922. After tracheal bouginage, the patient was discharged from the hospital as cured.

CASE 8.—*Hypertrophic Stenosis of the Larynx.*—A. B., a boy, aged 11 months, had been in the Essex County Isolation Hospital sixty-nine days prior to my first visit. In order to get rid of the intubation tube, tracheotomy was performed on May 6, 1924. After tracheal bouginage, the patient was decannulized on October 22. During this period the child had two attacks of bronchial pneumonia.

Subsequent History.—After decannulization, the infant did not seem to improve. On November 26, roentgenograms were taken and the report of the roentgenologist was: "There is evidence of a dense, circumscribed, infiltrated area involving the upper lobe on the right side. Below and near the hilum is another fair-sized, infiltrated, dense area of lung tissue. In the clear lung area there is slight mottling. There is fine and discrete mottling in the left pulmonary

Fig. 6.—Roentgenogram showing laryngostomy tube and rubber tubing in situ in case 5.

field. The right lung has the appearance of an old pneumonic lesion with a circumscribed, encapsulated effusion in the upper area. There is evidence of a tuberculous infection in both lungs."

The child gradually became worse and, on May 30, 1925, died of acute miliary tuberculosis.

CASE 9.—*Cicatricial Stenosis of the Larynx.*—R. S., a boy, aged 2, admitted to the Isolation Hospital on Nov. 16, 1922, had been in the hospital four months prior to my first visit, which was in March, 1923. Tracheotomy was performed on March 26, 1923, and the tonsils were removed on Oct. 27, 1924. The patient has had tracheal bouginage, but there has been very little progress made, mainly because of the lack of cooperation on the part of the family in not bringing the child to the hospital at regular intervals for treatment. It is now necessary to perform a laryngostomy, although at times the patient has been going for months with the tube completely corked up.

CASE 10.—*Cicatricial Stenosis of the Larynx Accompanied by Supraglottic Granulations.*—A. M., a boy, aged 1 year, was admitted to the Essex County Isolation Hospital on Feb. 21, 1922. I saw the patient for the first time on April 1. After numerous attempts were made to remove granulation tissue and tracheal dilatation by the O'Dwyer method, a tracheotomy was performed on June 15. The patient was treated by tracheal bouginage until July 6, 1923, at which time a tonsillectomy was performed. On August 23, the patient was decannulated, and at the present time has a small tracheotomic opening. Three attempts have been made to close this, but each time the closure has been postponed because of acute coryza. The patient has been decannulated for two and one-half years.

Fig. 7.—Laryngostomy opening after complete epithelization (case 5).

Fig. 8.—Plastic closure (case 5).

CASE 11.—*Hyperplastic Stenosis of the Larynx.*—A. S., a girl, aged 2, was admitted to the Essex County Isolation Hospital on Jan. 22, 1922, and had been in the hospital three months prior to my first visit, at which time supraglottic granulations were removed. The patient was treated without progress until May 18, when a tracheotomy was performed to get rid of the intubation tube. Subsequent history was uneventful, other than one attack of bronchial pneumonia during that year. On May 25, 1923, the patient's tonsils were removed and on June 28, she was decannulated. The tracheotomic opening was closed on June 26, 1925. Result: Cured.

Case 12.—*Hypertrophic Stenosis, Accompanied by Panic Stenosis of the Larynx.*—D. R., a boy, aged 3, was admitted to the Essex County Isolation Hospital on Feb. 18, 1922. He had been in the hospital one month prior to my first visit. Supraglottic granulations were removed, and attempts made at various times to extubate the patient were unsuccessful. In May, 1922, a tracheotomy was performed, followed by tracheal bouginage. On June 29, 1923, a tonsillectomy was performed, and the patient was decannulated on Oct. 22, 1924. At the time of writing the tracheotomic opening was closed. Result: Cured.

Case 13.—*Hypertrophic Stenosis of the Larynx.*—Q. D., a boy, aged 3, was admitted to the Essex County Isolation Hospital on Jan. 21, 1922. He had been in the hospital two months prior to my first visit. Various unsuccessful attempts were made to extubate the patient permanently, and on May 11, a tracheotomy was performed. Tracheal bouginage was carried on until May 4, 1923, when a tonsillectomy was performed. The patient was decannulated on June 28. In March, 1924, an attempt was made to close the tracheotomic opening with partial success. This was closed on Aug. 5, 1925. Result: Cured.

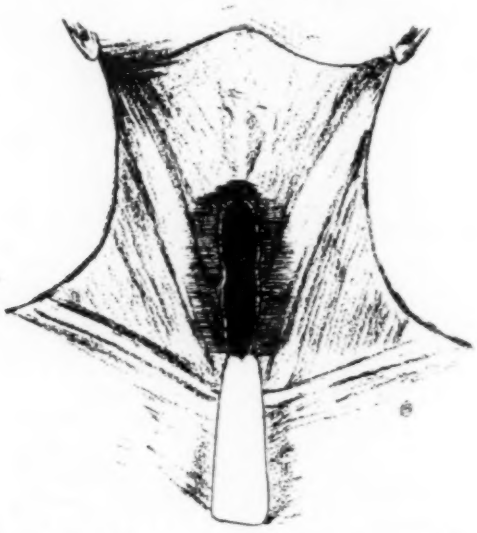

Fig. 9.—Schematic drawing of plastic closure of laryngostomy opening as practiced in cases 2, 4 and 5, procedure following closely that of Nassau.

Case 14.—*Cicatricial Stenosis of the Larynx.*—O. S., a boy, aged 6, was admitted to the Essex County Isolation Hospital in November, 1918. Tracheotomy was performed by Dr. Lynah on Dec. 17, 1919, and the patient was treated by him until the time of Dr. Lynah's death, when the boy was referred to me for further treatment, which consisted of tracheal bouginage. His tonsils had been removed some time previously by Dr. Lynah. On Sept. 6, 1923, the patient was decannulated, and at the time of writing there was still a slight tracheotomic opening but no discomfort and no untoward effects. Result: Cured.

Case 15.—*Cicatricial Stenosis of the Larynx.*—C. F., a girl, aged 19 months, was admitted to the Essex County Isolation Hospital on Dec. 27, 1924. She had been ill for three days with the diagnosis of laryngeal diphtheria, and at the hospital the diagnosis was confirmed; cultures were positive; streptococci were also present. On admission, antitoxin was given, and the intubation was performed with a rubber tube suitable for the age of 1 year, with little, if any relief. Reintubation was performed with a rubber tube suitable for the age

of 2 years, with immediate relief. The patient coughed up the tube frequently and was intubated eleven times during the first thirty-three days in the hospital. She went from four to eight hours without a tube. Feeling that this was a case of hypertrophic laryngeal stenosis and that the larynx should be at rest, Dr. Pringle performed a tracheotomy on Jan. 29, 1925. Subsequent to tracheotomy, the child did much better and gained in weight although she could not breathe properly with the tube corked. On March 31, the patient was referred to me, was treated by tracheal bouginage and was decannulated on October 8. Result: Cured.

CASE 16.—*Fibrous Stenosis of the Trachea.*—R. W., a woman, aged 28, was first seen by me on Oct. 21, 1924, with a history of having diphtheria at the age of 6 years. For some time previous to examination she had been troubled with difficulty in breathing and hoarseness. On laryngoscopic examination on October 22, a subglottic stenosis was seen. After the stenosis was cut and the trachea had been dilated five times, the patient was discharged on March 25, 1925.

CASE 17.—*Fibrous Stenosis of the Larynx.*—K. C., a girl, aged 7, was referred to me in June, 1923, with a previous history of diphtheria. The child was having

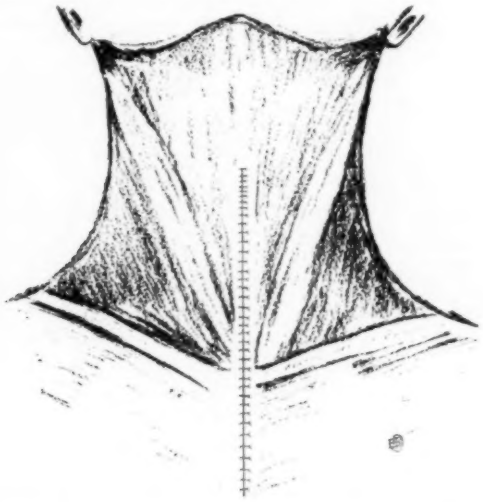

Figure 10.—Suture line after plastic closure.

some difficulty in breathing, and on direct laryngoscopic examination a fibrous band connecting both arytenoids was seen. This was cut, and after a few tracheal dilatations the patient was discharged. Result: Cured.

CASE 18.—*Fibrous Stenosis of the Trachea.*—A. G., a woman, aged 21, was first seen by me at the Polyclinic Hospital on Sept. 1, 1925, with a history of having diphtheria at the age of 6 years. During the last six months the patient has been treated by tracheal dilatation.

CASE 19.—G. S., a boy, aged 11 months, was admitted to the Essex County Isolation Hospital on Jan. 12, 1925. The patient had been ill for four days with laryngeal diphtheria and bronchopneumonia. His pulse was very irregular and weak, and the laboratory reports showed positive cultures in the throat. The patient was intubated immediately with only partial relief. The tube was frequently coughed up and the child was intubated six times. Tracheotomy was performed on Jan. 28, 1925, but the patient did not do well and died on February 12 from toxemia.

CASE 20.—C. S., aged 14 months, was admitted to the Essex County Isolation Hospital on Feb. 13, 1925. The patient had been ill three days with laryngeal diphtheria and was intubated with immediate relief. Antitoxin was given; all cultures were negative. The patient was intubated eleven times, extubated six times, and coughed up the tube five times. A tracheotomy was performed on March 20, and on April 7, the tube was partially corked and the patient did well. On April 9, the tube was fully corked and the patient's breathing was fairly easy. The tracheotomy tube was removed on April 24; the wound healed entirely, breathing was easy and the patient was discharged from the hospital on May 7. Result: Cured.

CASE 21.—M. C., aged 1½ years, was admitted to the Essex County Isolation Hospital on March 17, 1925. The patient had been ill two days with laryngeal and bronchial diphtheria; was intubated with little, if any, relief, and a tracheotomy was performed on March 18. The cultures were negative. The patient died on March 19 from toxemia.

CASE 22.—A. L., aged 2½ years, was admitted to the Essex County Isolation Hospital on Feb. 17, 1925. The patient had been ill for two days with laryngeal diphtheria and bronchopneumonia; she was intubated with partial relief, but did not do well. Intubation was performed six times and tracheotomy was performed on March 22 but the child died the next day. Cultures were negative.

Fig. 11

Fig. 12

Fig. 11.—Photograph taken two years after operation (case 1).
Fig. 12.—Photograph taken one year after closure (case 12).

CASE 23.—A. H., aged 22 months, was admitted to the Essex County Isolation Hospital on Aug. 29, 1925. The patient had been ill for four days with laryngeal diphtheria and pneumonia and was intubated with only partial relief. The throat was highly inflammatory and edematous. Culture was positive for diphtheria. The patient was intubated three times and a tracheotomy was performed on September 12, and a 2 year Jackson tube was inserted. The child did very well and on October 21, the tube was corked. On November 12, the tube was removed and the patient was discharged from the hospital on November 29 as cured.

CASE 24.—M. M., aged 1 year, was admitted to the Essex County Isolation Hospital on June 8, 1925. The child had been ill for two days with laryngeal diphtheria and bronchopneumonia; intubation was done and 20,000 units of antitoxin and oxygen were given; a culture was negative, and a roentgenogram for foreign body obstruction was also negative. The patient was intubated fifteen times and extubated eleven times; the tube was coughed up five times, and the patient became cyanotic and pulseless quickly. Tracheotomy was done August 26 and a 1 year Jackson tube was inserted. The patient would go for three and four days with the tube corked up tightly. The tube was removed on November 13, and the patient did well until November 23, when the tube had to be reinserted. The patient was transferred to the Newark City Hospital and is now under my care.

CASE 25.—E. M., aged 5 years, was admitted to the Essex County Isolation Hospital on Nov. 2, 1925. The patient had been ill for four days with laryngeal diphtheria and was intubated immediately with a four to five year rubber tube. Antitoxin was given, and cultures were negative. In this case there was a history of a foreign body a few days before illness, but a roentgen-ray examination was negative for a foreign body. The patient was intubated twice and could not go at all without the tube, therefore a tracheotomy was performed on November 17. Many attempts were made to cork the tube, but the patient could not breathe properly with it corked. On Jan. 7, 1926, the patient was transferred to the Eye and Ear Infirmary and is now under my care.

CONCLUSIONS

Because of the long time necessary for treatment of these cases before they can be decannulized, should we not urge early tracheotomy in diphtheria rather than await the uncertain procedures of continued intubation?

The constant wearing of intubation tubes causes changes within the larynx.

The larynx will tolerate with less irritation apparatus covered with Penrose tubing.

Before any attempt was made to decannulate these patients, infected tonsils were removed. The influence of disease in all laryngeal cases is important, and the diseased tonsils, as well as any nasal infection, should be eliminated before any work is attempted.

Clinical Note

THE IMPROVED ENDOSCOPE FOR CLOSING SAFETY-PINS*

A. J. SHEKTER, M.D.
JAMAICA, L. I.

The instrument presented is the modification of my original one, previously described.[1]

Instead of having the light carrier channel (A) fixed to the sight tube (B) as in the original endoscope, it is here made movable, thereby serving the combined purpose of acting as a channel for the light carrier and as a lever for manipulating the safety-pin closing loop, thus permitting an entirely free sight tube in which to work.

Fig. 1.—Point up safety-pin in the esophagus of dog.

The instrument as it is, can be used not only for the purpose of closing safety-pins or extracting flat objects, especially the smooth kind that are hard to grasp with forceps, but also as a regular endoscope for diagnosis and treatment when the 4, 5 and 7 mm. tube is required.

When drawn down, the loop has the same circumference as the sight tube, thus eliminating any visual obstruction. The only additional instrument used in closing and extracting the pin is the prong.

The roentgenograms show the various steps taken in extracting the point up safety-pin in the esophagus of a young dog (under ether anesthesia).

*The instrument in three sizes (4, 5 and 7 mm.) is made by Pilling, Philadelphia.

1. Shekter, A. J.: A New Endoscope for Closing Safety-Pins, Arch. Otolaryng. **1**:643 (June) 1925.

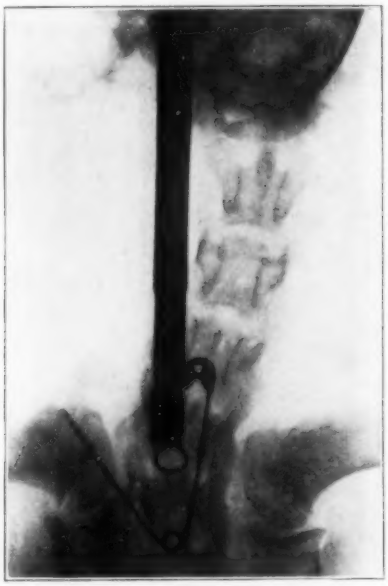

Fig. 2.—Instrument introduced with loop closed till cricopharyngeus is passed, then loop drawn up and spring coil of pin sighted.

Fig. 3.—Endoscope pushed farther down, so that spring coil of pin with its side arms passes between both blades of tube.

Fig. 4.—Loop now drawn down and locked, tube now withdrawn slightly so as to engage spring coil of pin into loop.

Fig. 5.—Prong now introduced, pushing spring coil of pin through loop, which at the same time draws both arms of pin into slit on each side of tube. Tube pin and prong are then withdrawn.

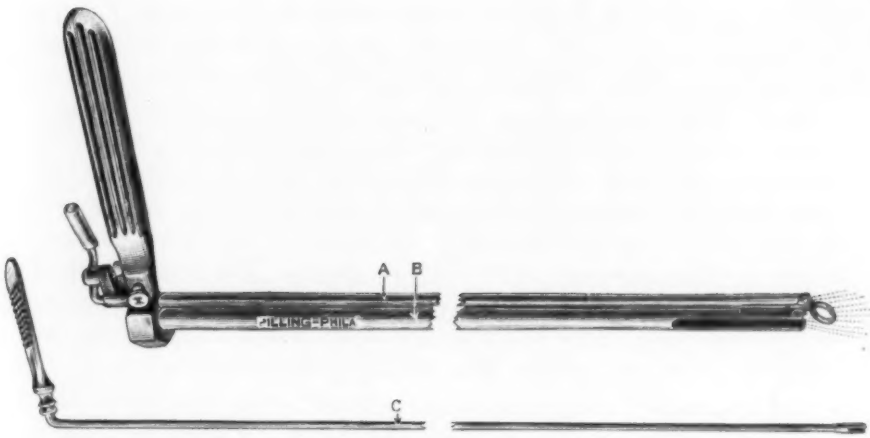

Fig. 6.—Improved endoscope.

Progress in Otolaryngology

A Summary of the Bibliographic Material Available in the Field of Otolaryngology

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CHRONIC PROGRESSIVE DEAFNESS

INCLUDING OTOSCLEROSIS AND PATHOLOGY OF THE INNER EAR

J. K. M. DICKIE, M.D.
OTTAWA, ONT.

In a study of otosclerosis, Meyer [1] compares the development of the labyrinth capsule with that of the long bones. Up to the period of the development of the marrow space in the long bones, the process is much the same; from that point the similarity ends. In the long bones there is complete absorption of the cartilaginous pillars to form the large marrow spaces. In the labyrinth capsule, on the other hand, there is a continuous deposition of layers of lamellar bone without previous absorption of the cartilage, making it extremely compact. In the long bones no trace remains of the embryonic structures, but in the labyrinth capsule numerous vestiges of cartilage are found. The most important difference is that in the long bones changes are going on during the whole of life, while in the labyrinth capsule growth is completed by the end of the second year and remains stationary thereafter.

BLOOD CHEMISTRY

During the past year, a considerable amount of research has been carried out on chemistry of the blood in relation to otosclerosis. According to Leicher,[2] serum diagnosis as yet shows nothing very characteristic in otosclerosis, but there is a decided similarity in the analysis of the blood serum in otosclerosis and cancer. In his researches, only cases of undoubted cancer and otosclerosis were used. He found that the calcium content of the serum, which in normal cases ranges from 10.9 to 12 mg. per hundred cubic centimeters, is slightly lowered. Out of three hundred cases of otosclerosis 80 per cent showed the calcium content between 9.8 and 10.8. Out of twenty-one cases of cancer eighteen had figures between 9.9 and 10.8. With regard to carbohydrate metabolism, there is usually a normal percentage in otosclerosis, but the sugar tolerance is lowered in both otosclerosis and cancer. The

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1. Meyer, M.: Passow-Schäfers, Beitr. **21**:1-6.
2. Leicher, H.: München. med. Wchnschr. **72**:762 (May 8) 1925

cholesterin in the serum is less than normal in both. The albumin-globulin ratio shows in both diseases a relative increase in globulin. The Kahn test gave a positive reaction in eight out of twelve cases of otosclerosis and the results were similar in cases of cancer. The antitryptic serum titer is indefinite. He concludes that the findings are in no way specific, as similar results are obtained in other conditions, but are characteristic enough to deserve comment. Berberich [3] determined the blood cholesterol in thirty patients with otosclerosis. All but one had very low figures, from one-half to one-tenth normal. Two of the patients were near the term of pregnancy, when normally cholesterols increase in the blood and disappear from the ovaries. He quotes Fleischmann as having found similar low cholesterol figures in ozena. Other degenerative conditions also have low cholesterol figures.

BLOOD CALCIUM CONTENT

Kopetzky and Almour [4] investigated the calcium content of the blood in twenty patients suffering from various forms of deafness. The majority were cases of otosclerosis. Of the twenty cases fourteen showed a diminution of blood calcium, and in ten of these fourteen a clinical diagnosis of otosclerosis had been made. The diagnosis had been based on (1) heredity; (2) influence of pregnancy and infectious diseases on hearing; (3) prolonged bone conduction; (4) raising of the lower tone limit. In eleven of the twelve patients in whom the condition was diagnosed as otosclerosis, the calcium content of the blood was altered from the normal. The presence of an alteration of the calcium content in the blood examined after a fasting period of several hours is strong corroborative evidence of the presence of otosclerosis in a patient who presents a loss of hearing clinically, and a history of deafness in one or more blood relatives.

PREGNANCY AND OTOSCLEROSIS

Discussing the effect of pregnancy on otosclerosis Stein [5] states that a latent otosclerosis can undoubtedly be stirred up by pregnancy, especially if it is the first. He attributes this to the disturbing effect of pregnancy on the internal secretions. He considers that when the hearing is already fairly poor in one ear, or slightly impaired in both, abortion is indicated. It is also indicated if there are symptoms of early involvement of the labyrinth, or if there is a strong hereditary tendency to otosclerosis. When there is marked cardiovascular disturbance or

3. Berberich, J.: Klin. Wchnschr. **3**:2003 (Oct. 28) 1924.

4. Kopetzky, S. J., and Almour, R.: Blood Calcium in Undifferentiated Deafness, Arch. Otolaryng. **1**:473 (May) 1925.

5. Stein: Monatschr. f. Ohrenh. **59**:5 (May) 1925.

signs of derangement of internal secretion, such as tetany, glycosuria, etc., abortion should be performed. Alexander,[6] discussing the same subject, gives four indications for abortion. They are: (1) in a case of otosclerosis which is in itself unfavorable as regards prognosis; (2) in otosclerosis in which there is deafness on both sides; (3) when the patient is pregnant for the second time and is not over 25 years of age; (4) in otosclerosis associated with unfavorable social conditions. He also advises abortion in any middle ear suppuration, especially if tubercular. If the local condition becomes worse, or if an intracranial complication shows itself, it is also indicated.

INFLUENCE OF SEXUAL DEVELOPMENT ON OTOSCLEROSIS

Stein,[7] in a paper on the influence of sexual development and abnormal sex life on otosclerosis, emphasizes its predominance in the female sex and the influences of menstruation, gravidity, climacteric, etc., on the course of the disease. In many of his cases the onset could be traced to the first pregnancy, and the hearing generally improved after parturition. He investigated the sex life of 125 patients with otosclerosis, 68 per cent of whom were women. The symptoms began at puberty in 27.1 per cent. There had been abnormal menstruation in 36.5 per cent. The progress had been more rapid in these patients than in those with normal menstruation. An unsatisfactory sex life, and especially coitus interruptus, were mentioned as probable causes by many patients. With regard to the males, many gave a history of sexual neurasthenia, impotence, frigidity and other derangements of sexual function, while of ten patients who had suffered from otosclerosis since puberty, two had hypospadias, and one had hypoplasia of the genital organs. He regards otosclerosis as a degenerative state associated with disturbances of the internal secretions. Patients must be treated individually according to the abnormality in question.

Jousseaume[8] writes in much the same strain, namely, that nearly all true cases of otosclerosis occur in women, and that the ductless glands cause a greater metabolic fluctuation in women than in men. Puberty, menstruation, pregnancy, lactation and the climacteric cause great changes in endocrine function. The development of otosclerosis varies with the function of the ovaries and pituitary. Otosclerosis commences at puberty, advances during pregnancy and improves after the menopause. He investigated the basal metabolism in five selected cases of undoubted otosclerosis. In all five cases the basal metabolism was definitely low. Four of the five were girls of 14 to 16 years of

6. Alexander: Monatschr. f. Ohrenh. **59**:1 (Jan.) 1925.
7. Stein, K.: Wien. klin. Wchnschr. **38**:3, 1925.
8. Jousseaume, R.: Ann. d. mal de l'oreille, du larynx (Jan.) 1925.

age, and the fifth was a woman, aged 33, and in all of them the condition started at puberty. In one case menstruation was normal, but in the others the flow was increased.

With regard to treatment, the author advises administration of phosphorus, calcium and fluorine and also pituitary extract.

OTOSCLEROSIS AS A DISEASE

Lake,[9] in an interesting paper, questions the correctness of regarding otosclerosis as a distinct disease. He states that while the pathologic condition bearing the name is quite definite, the clinical condition is not so well defined. With reference to etiology he states: "Heredity in otosclerosis is, I think, not proven, unless we are prepared to consider all nonsuppurative middle ear affections not as potential but as actual otosclerotic cases." He groups together, as being all associated with sepsis, other conditions which are are said to be contributing factors in the production of otosclerosis, such as rheumatism, gout, anemia, rickets, etc. The symptoms which are usually accepted as pathognomonic of otosclerosis are Bezold's triad, namely, loss of low tones, prolonged bone conduction, and a negative Rinne test, as well as tinnitus and paracusis. These signs are all found in other conditions, such as chronic catarrh with eustachian tube obstruction and middle ear suppuration.

Discussing treatment, Lake affirms that a patient with deafness of the before-mentioned type who is cured or recovers, can hardly have true otosclerosis, as it is almost inconceivable that the well-known pathologic changes could be removed by any kind of treatment as yet known. All septic foci must, of course, be thoroughly eradicated.

In summing up his observations he concludes: "Briefly, certain changes have been found in the temporal bone, and around them has been erected a disease. Is this justifiable? I think not." The results of treatment show whether a given case is one of otosclerosis or not.

HUMORAL DEAFNESS

Claoué [10] has described a condition which he designates humoral deafness, in which the clinical signs are those of otosclerosis, but in which there is no family history of deafness. The onset is rapid and there is a diminution or loss of excitability of the vestibular apparatus. By analogy with the eye, in which variations in intra-ocular pressure have an effect on vision, Claoué argues that deafness may be caused by changes in labyrinthine pressure. The stria vascularis may be compared with the ciliary body in its regulation of fluid pressure. He

9. Lake, R.: J. Otol. & Laryng. **40**:512 (Aug.) 1925.

10. Claoué, R.: L'oto-rhino-laryngologie Internat. (July) 1924.

explains on this basis those cases in which the clinical signs are those of otosclerosis, but improvement or cure occurs in the patient. Particulars of a case are quoted in which there was no family history of deafness, but a bad prognosis had been given. However, improvement occurred with constitutional treatment.

TYMPANIC PRESCLEROSIS

Calderin [11] contributes an article on the so-called tympanic presclerosis of Citelli. It is a condition occurring in older children with adenoids, in whom there is an impairment of hearing which is not improved after adenoidectomy, but rather the reverse. There is very little to be seen locally to account for the deafness, but there is generally a family history of otosclerosis and the condition is regarded as one of impending otosclerosis. The treatment recommended is the administration of calcium, iodine and peptone.

DEAFNESS AND BIRTH TRAUMA

Voss,[12] writing on injury to the hearing organ from birth trauma, contributes some interesting facts. Starting from the fact that the brains in 65 per cent of stillborn infants show macroscopically intracerebral bleeding, he undertook to investigate the hearing and balancing functions of infants to discover if the intracranial tracts associated with them were affected. A large number of infants and older children were examined, and disturbances of audition and balancing were found in a fair proportion. In most cases there was a return to normal later. That all the lesions were probably not in the brain itself was shown by the finding of congested vessels and hemorrhages in the labyrinth of stillborn children. Voss argues from these facts that it is pretty certain that some cases of congenital deafmutism are caused by birth trauma.

VASOMOTOR INNER EAR DISTURBANCES

Brunner [13] contributes an article on vasomotor disturbances of the inner ear. He mentions as exciting causes neurasthenia, migraine and the climacteric, as well as poisons such as nicotine and alcohol. He carried out some experimental work on guinea-pigs. Since concussion of the head produces dilatation of the blood vessels of the brain, and as the blood vessels to the labyrinth come from the circle of Willis, he reasoned that there would be dilatation of the labyrinthine vessels. Accordingly, he subjected guinea-pigs to blows on the head so as to

11. Calderin: Rev. españ. de laringol. **25**:220, 1924.
12. Voss: Centralbl. f. Ohrenh. **24.**
13. Brunner, H.: Wien. klin. Wchnschr. **38**:1235 (Nov. 12) 1925.

produce commotio, and subsequently examined the ears microscopically after killing the animals by bleeding. The vessels in the inner ear were found to be dilated, with here and there around them eosin-staining exudate containing a few leukocytes. The endolymph and perilymph spaces showed some hemorrhages and also curdled lymph. The sense epithelium everywhere was intact. This is said to show that vascular disturbances may cause organic changes.

Schmierer [14] discusses the reddish glow from the promontory which is thought to be pathognomic of otosclerosis, and points out that it is sometimes seen in persons with normal hearing, especially degenerates and cretins. The anatomic substrate is dilated vessels.

PARACUSIS

Kranz [15] contributes a paper on the question of paracusis. He subjected a number of patients with paracusis to various tests with noise-producing apparatus. He comes to the conclusion that the hearing under these circumstances is actually no better than usual, but the apparent improvement in hearing is due to the voice being raised. Another point is that the noises are generally sounds of low frequency which are not heard by the patients, and therefore do not disturb them.

TREATMENT OF HEAD NOISES

With regard to the treatment of subjective head noises, on the assumption that the noises were due to angiospasm, Brüning and Forster [16] reasoned that removal of the cervical sympathetic ganglions would stop the noises. This was tried in one patient to whom the noises had become so unbearable that suicide was threatened. The ganglion stellatum and the lower pole of the supreme ganglion with the intervening strands, as well as the sympathetic fiber surrounding the carotid, were removed. The ganglion stellatum was removed in order to interrupt the fibers that accompany the vertebral vessels. After the operation the vessels over the whole side of the head were dilated. The noises did not cease immediately although there was a great improvement. At the end of three months the noises had gone and the patient had gained in weight.

A similar case is reported by Rubaschow,[17] but with not so good a result. The patient was a woman, aged 35, who was very much troubled with head noises. All three ganglions were removed on the right side.

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14. Schmierer: Monatschr. f. Ohrenh. (Nov.) 1924.

15. Kranz: Ann. Otol., Rhin. & Laryng. **33**:283 (March) 1924.

16. Brüning, F., and Forster, E.: Deutsch. med. Wchnschr. **51**:860 (May 22) 1925.

17. Rubaschow, S.: Deutsch. med. Wchnschr. **51**:1667 (Oct. 2) 1925.

After the operation, Körner's symptom-complex was very definite. In the first two months the head noises were very much lessened but they came back in three months. The hearing was improved after the operation, but later returned to the same condition as before.

AUDITORY REEDUCATION

The question of auditory reeducation by the method of Zünd-Bourguet has been reopened by Cathcart.[18] This method had never attained any popularity, as on theoretic grounds it did not show any reasonable prospect of cure, and at the same time the extravagant price demanded for the apparatus made any trial rather an expensive luxury. Cathcart gives details of 100 patients with incurable chronic progressive deafness treated by this method. Every patient in the series had consulted at least two other otologists before being treated. The cases were grouped as follows: nerve deafness, 34; chronic otitis media, 33; otosclerosis, 33. Sixty-eight per cent showed actual improvement, and of these 81 per cent in the first group, 67 per cent in the second, and 55 per cent in the third group. The only test for hearing used was the whisper with residual air, which the author claims to be able to make pretty constant in intensity. Tinnitus was improved, although independently of the hearing. If after twelve trial treatments there is no improvement, the author states that it is not worth while to continue. As a rule, thirty séances are enough, but the course of treatments must be repeated in from six to nine months. In many instances the improvement in hearing was said to have lasted over a year. Details of the hearing are given in each case.

Cathcart concludes: "The improvement in so large a proportion of patients, every one of whom had already been treated by the ordinary methods and pronounced incapable of improvement, cannot be lightly dismissed as a mere manifestation of suggestion or autosuggestion.

"As regards tinnitus, the records above show that this treatment not only alleviates it, but often causes it to disappear completely. It is not an exaggeration, therefore, to claim that the electrophonoide treatment, when properly carried out, can and often does cure tinnitus."

Salinger[19] has reported adversely on the results of treatment on similar lines. Experiments on auditory reeducation were carried out with a sound amplifying device containing a vacuum tube amplifier. All the tests were carried out by the same person, and the final test was made without looking at the records. Forty-eight patients were exam-

18. Cathcart, G. C.: The Treatment of Deafness by the Acoustic Method, Lancet **1**:968 (May 9) 1925.

19. Salinger, S.: Arch. Otolaryng. **1**:397 (April) 1925.

ined, but only sixteen persisted with the treatments. Of these, two were improved, eight were worse, two showed no change and four were doubtful.

He concludes that there is a danger of permanently damaging the acoustic apparatus through prolonged irritation by the loud sounds which the machine conveys.

Harris [20] reports good results in the treatment of chronic progressive deafness with the galvanic current. The negative pole causes hyperemia, local elevation of temperature and absorption of scar tissue. The external meatus is filled with gauze soaked in sodium chloride, and the negative pole is applied. The positive pole is supplied by a copper spatula in the mouth. The current is gradually turned on to the limit of tolerance but not to exceed 2 milliamperes. It is allowed to flow twenty to twenty-five minutes and then a sinusoidal current is applied for five minutes. Treatment is carried out every other day. Immediately after treatment, the upper half of the drum is congested and the patient has a feeling of well-being. Of eleven patients treated, nine were improved, especially in respect to tinnitus.

Several authors have discussed roentgen-ray treatment of otosclerosis and progressive deafness. Frey and Kriser [21] report improvement in the head noises in eight out of thirty-eight cases of otosclerosis. The hearing was also improved. They apply the rays to the pituitary, and also to the thyroid and parathyroids on the assumption that it is an endocrine disturbance.

Grande [22] also reports the results of treatment with roentgen rays on twenty-three patients with deafness of various types. Fifteen cases of catarrhal otitis media were treated, and improvement was noted in all, both as regards hearing and tinnitus. Five patients with otosclerosis were treated, with no result whatever in three, and with improvement of the tinnitus in two but without improvement of the hearing. In one of these, the otosclerosis was of a very bad type in a young married woman, in whom the condition was apparently arrested in spite of pregnancy. In short, Grande's results agree fairly well with those of previous writers, in that catarrhal otitis media is likely to benefit considerably, while otosclerosis and nerve deafness are not.

Linn [23] recommends diathermy in chronic middle ear catarrh and otosclerosis.

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20. Harris, M. L.: Laryngoscope **35**:9 (Jan.) 1925.
21. Frey and Kriser: Ztschr. f. Hals-, Nasen.-u. Ohrenh. **6**:2, 1924.
22. Grande, C.: Arch. ital. di otol. **36**:197, 1925.
23. Linn: J. Radiol. **6.**

TREATMENT WITH DRUGS

As regards drug treatment, Beck [24] has obtained beneficial results by giving strychnine in vertigo, tinnitus, and objective derangements of equilibrium. The hearing is improved in some instances. Disturbances due to vasomotor abnormalities respond especially well to strychnine. The initial dose should be from 1 to 2 mg. daily, increasing by 1 mg. up to 6 mg. daily, and then decreasing again to 1 mg.

German and Kelemenz [25] report some very encouraging work on nerve deafness. Forty-two patients were examined, eighteen of whom showed an excess of uric acid in the blood. The normal maximum is 3.5 mg. per hundred cubic centimeters of blood after three days of purin-free diet (Folin-Neubauer method). All were patients in whom other possible etiologic factors such as syphilis, trauma, nicotine poisoning, etc., were excluded. Twelve patients had other symptoms of gout, such as arthritis, and were put on a purin-free diet. Nine of these were later retested, and showed a return to normal. Of these, four improved greatly in hearing, four were unchanged, four reported tinnitus greatly improved, two had improvement in vertigo and one of insomnia caused by tinnitus. Of three patients who were not retested for uric acid, one did not return, one reported relief from headache, noise and vertigo, and one improved in hearing in one ear only. The only patient of the nine who was not relieved was one in whom the blood uric acid remained above normal (4.4 mg.). In most of the patients the symptoms had been of many years' duration.

Uspenskaja [26] draws attention to the fact that a basal gummatous meningitis may be the cause of a high grade deafness coming on in a tabetic subject. A case of this type is reported.

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24. Beck: Ztschr. f. Hals-, Nasen.-u. Ohrenh. **9**:222, 1924.

25. German and Kelemenz: Ztschr. f. Hals-, Nasen.-u. Ohrenh. **10**:175 (Nov.) 1924.

26. Uspenskaja, V.: Ztschr. f. d. ges. Neurol. **95**, 1925.

CORRECTION

In discussing the paper by Dr. George E. Shambaugh, an abstract of which appears in the Proceedings of the Chicago Laryngological and Otological Society (*Arch. Otolaryng.* **3**:297 [March] 1926), Dr. Charles W. Richardson referred to the work of Dr. W. Scott Renner, Buffalo. Dr. Renner's name was through error given as "Rinder."

Correspondence

"FUNCTIONAL EXAMINATION OF HEARING"

To the Editor:—Friendly criticism stimulates scientific accuracy in the statement of alleged facts, and so Dr. Sonnenschein's criticism,[1] on page 64 of *The Archives of Otolaryngology*, of the statement made in the article by Wegel and me on the audiometer, calls for a friendly reply and acknowledgment on my part, for I am responsible for the statement under indictment.

The criticism does not alter my belief in the least that my statement is true, and that it is also easy of comprehension. However, I am willing to acknowledge that the statement may be considered sketchy and therefore in need of elaboration, so that the essential truth may be readily understood and accepted by every reader.

The paragraph under discussion is as follows:

"In cases of impaired hearing due to obstruction of the auditory canal, the chart-curve will show the greatest drop in the low tones in cases of simple type. The fineness of the audiometer record is such that it suggests in some cases of this nature an irritable auditory nerve (probably an initial congestion incident to a possible eustachian tube factor). In such cases the chart-curve for high tones may also show quite a drop and disappear promptly after the removal of the offending obstruction to the canal, for the complicating eustachian tube factor will recover spontaneously on the removal of the obstructing pathology in the external auditory canal."

Analysis of the paragraph reveals three essential statements, namely: First, that in cases of impacted cerumen the hearing tests, as recorded by the audiometer, show the greatest drop for low tones in cases of *simple type*. This truly accords with accepted teaching that obstructive deafness causes the greatest loss for low tones. Therefore, it would seem that this statement requires no further explanation, for it refers to the *uncomplicated type of obstruction in the external auditory canal*, due to impacted cerumen or furuncles.

The second item in the paragraph has to do with an "irritable auditory nerve." In explanation of the use of the term "irritable" associated with loss in sensitivity to various tones, it was my purpose to indicate nerves in a state of partial exhaustion sequent to a long continued, venous stasis. The word *irritable* refers to a likely *early pathology* of a normally sensitive nerve. The effect on hearing acuity is loss for both low and high tones which, except in the presence of syphilis, is simply a functional disturbance and promptly disappears on removal of the causal agent, namely, obstructing substance in the external auditory canal.

The cochlear endings of the nerve are known to be physiologically *sensitive*, and must be so in order to appreciate the fine differences of pitch so necessary to normal hearing.

The cochlear endings of the eighth nerve may be likened to the retina, which also is known to be physiologically sensitive in a state of health, but which, for one reason or another, may become "irritable," and when in such a state the very first expression or evidence of a possible pathology may be photophobia, and in the neurasthenic or hysterical patient may sometimes be associated with concentric contraction of the visual fields. These eye findings may be considered analogous to the *initial* loss for both *low and high* tones incident to a functional irritability of the normally sensitive cochlear nerve endings.

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1. Sonnenschein, Robert: Progress in Otolaryngology, Arch. Otolaryng. **3**:60 (Jan.) 1926.

The perimetric findings and the audiometer records are both valuable in demonstrating functional disturbance before the onset of positive pathology.

The expression — "fineness of the audiometer record" — merely refers to the accuracy of the instrument in determining slight changes in function revealed by those tests before gross pathology is evident.

"The fineness of the audiometer record is such that it suggests in some cases of this nature an irritable auditory nerve (probably an initial congestion incident to a possible eustachian tube factor)." The possible eustachian tube factor which I had in mind was the collapse of the walls of the tube with resulting stenosis, *not stricture of the tube.* That this is a fact I have many times proved by the use of the catheter and bougie for relief of this condition *when present as a complication of obstruction to the external auditory canal* due to impacted cerumen or to other substance.

The collapse of the walls of the eustachian tube is due to vascular disturbance which affects the middle ear and very likely the vascular state of the entire labyrinth, and through the medium of the round window there is a natural explanation for subnormal appreciation of high tones. This condition, as it affects the tympanic cavity, may well be likened to the state of negative air pressure observed in the accessory nasal sinuses, for in such cavities there is always a venous stasis, and in the instance of obstruction of the external auditory canal, I have noted that there is frequently associated venous stasis affecting primarily the eustachian tube and middle ear, and secondarily the labyrinth. It seems to me that the changes noted are natural results of physical laws in action.

J. Ivimey Dowling, M.D., Albany, N. Y.

REPLY TO DR. DOWLING

To the Editor:—The spirit of the review was a most friendly and candid one. Some of the points raised by Dr. Dowling rather surprised me, but if I am mistaken, I am always glad to stand corrected. I stated in the article in the *Archives:* "It is possible that the signs of an inner ear involvement might be caused by a firm plug of cerumen which is pressing very firmly against the drum membrane, with pressure on the ossicles and the footplate of the stapes, as in a positive Gellé test. After removal of the cerumen, of course, all signs of inner ear involvement should be gone. However, the presence of obstruction in the external auditory canal could not very well produce eustachian tube involvement so far as I can see; as a rule, this is most likely to arise by way of the pharynx or nasopharynx."

Now, it is agreed that uncomplicated obstruction of the external meatus usually gives the findings of the conduction type of impaired hearing, but I ask what proof Dr. Dowling has for the assumption that the plugging of, or obstruction in, the external auditory canal produces symptoms in the eustachian tube, a structure which has an entirely different blood supply. Furthermore, what proof is there that a venous stasis of the eustachian tube, such as he assumes, can in any way produce similar changes of circulation in the labyrinth of the ear? There is surely every reason to believe that it could not have such an effect, as the blood supply of the labyrinth of the ear is a separate structure. I believe that reference to the well known classical work of Dr. Shambaugh on the circulation of the inner ear will throw much light on this subject.

With reference to the question of an "irritable auditory nerve," Dr. Dowling first discusses it as a phenomenon of exhaustion in which there is resulting defective hearing. Then he compares it with a hypersensitive condition of the retina in which a photophobia results which is a directly opposite condition. One is that of a hypersensitive state, and the other is that in which there is

a diminished sensitiveness of the nerve. We believe that physiologically a nerve must be irritable in order to respond to stimuli of various kinds.

There was no intention on our part to question "the fineness of audiometer records." The audiometer is an instrument of precision, but it does not necessarily follow that "it suggests in some cases of this nature an irritable auditory nerve (probably an initial congestion incident to a possible eustachian tube factor)" as Dr. Dowling states. As a matter of fact, with a few properly used forks it is easy to determine the beginning loss of hearing for high tones.

In order to warrant the various statements regarding the relationship of the tube to the labyrinth, etc., it seems to me that more definite proof might have been offered by the author in his original article.

ROBERT SONNENSCHEIN, M.D., Chicago.

News and Comment

LOCAL SOCIETY MEETINGS

BALTIMORE: The Section on Otology and Laryngology, of the Baltimore City Medical Society, meets on the last Friday of each month, at 1211 Cathedral Street, at 8:30 p. m. Chairman, Dr. Edward A. Looper; Secretary, Dr. Edwin N. Brayles.

CLEVELAND: Ophthalmological and Otolaryngological Section of Cleveland Academy of Medicine meets on the fourth Friday of each month at the Winton Hotel. Chairman, Dr. E. W. Garrett; Secretary, Dr. M. Paul Motto, Rose Building.

MILWAUKEE: Milwaukee Oto-Ophthalmic Society meets on the third Tuesday of the month, at the University Club, at 6:30 p. m. President, Dr. John E. Guy; Sec.-Treas., Dr. John J. Brooks, Majestic Building.

PHILADELPHIA: Section on Otology and Laryngology of the College of Physicians of Philadelphia meets on the third Wednesday of each month from October to June, at 8:30 p. m., at the College of Physicians. Chairman, Dr. Fielding O. Lewis; Secretary, Dr. James A. Babbitt, 2117 Chestnut Street.

Abstracts from Current Literature

Ear

BLUE DISCOLORATION OF THE SCLERAS AND FOCAL DISEASE OF THE LABYRINTHIAN CAPSULE. EDWARD GIMPLINGER, Ztschr. f. Hals-, Nasen- u. Ohrenh. **13**: 345 (Jan. 18) 1926.

The histology of bone changes in the labyrinthian capsule in otosclerosis has been made clear by a great number of investigators. Only the explanation and evaluation of the findings furnish fundamental differences which cannot be solved by histology. The relation of the local to the general condition of the individual comes to the fore in considering the disease. According to Alexander, the histologic findings point to the congenital nature of the first layer of the osseous changes. O. Mayer assumes that embryonic tissue malformations are the cause of the blastoma-like character of the focal disease. Brunner and Fischer adduce proofs concerning the correctness of the opinion that an inferiority of the hearing organ exists in otosclerosis. Hammerschlag proved that the disease is hereditary. The inferiority of the hearing organ is only a part of the general inferiority. J. Bauer and C. Stein showed in otosclerotics the constant occurrence of a number of defects of development and signs of degeneration. The focal disease can be accompanied by constitutional diseases which can be shown to be hereditary either as such or in alternations. The simultaneous occurrence of osteopsathyrosis, blue scleras and focal disease furnishes such a complex. The author reports the histologic examinations of the labyrinth of a patient belonging to this group. The vessels were very delicate and narrow. The histologic examination of the aorta showed very thin layers of the wall. The patient was a woman, aged 54, who did not show any signs of arteriosclerosis. J. Bauer considers the excessive delicacy of the walls and of the intima of the large vessels a part symptom of a degenerative status. The prevalence of eosinophils is a symptom of a constitutional anomaly. Otosclerosis, according to O. Mayer, is also related to another disease of the bone which is explained by constitutional factors, namely, ostitis deformans (Paget). Otosclerosis is placed in a complex of symptoms which point to a degenerative condition of the individual. This degenerative factor consists of an anomaly of the constitution of a whole tissue group, the mesenchyma. All changes, like blue scleras, osteopsathyrosis, ostitis deformans, tissue hypoplasia and otosclerosis are to be referred to the mesenchyma. Gimplinger thinks that the constitutional nature of otosclerosis should, at least, be considered in the sense that constitutional inferiority of the mesenchyma can be assumed in people suffering from otosclerosis, and that the focal disease is only a manifestation brought about by causes still unknown.

AMBERG, Detroit.

Larynx

THE INDIRECT EXAMINATION OF THE LARYNX ESPECIALLY OF THE MOST ANTERIOR PARTS OF THE SAME WITHOUT PROTUSION OF THE TONGUE. EUGEN POLLAK, Ztschr. f. Hals-, Nasen- u. Ohrenh. **13**:353 (Jan. 18) 1926.

Moriz Schmidt mentioned that it is frequently surprisingly easy to obtain a view of the larynx if the tongue is depressed by a spatula and not protruded. Tuerck also mentioned that an examination at times is more successful, at

least to a certain degree, if the tongue is not protruded. Manuel Garcia, in his examinations, did not interfere with the position of the tongue. Pollak states that the indirect laryngoscopy without protrusion of the tongue is possible in 80 per cent of the people. With a Fraenkel or Baginsky tongue depressor the tongue is gently pressed down, while the laryngeal mirror is introduced in the usual manner; the patient says "ae." When "e" is pronounced, the view into the larynx becomes better. Pollack found that his method was successful in some cases in which the usual method was unsuccessful, and that it made inspection of the most anterior parts of the larynx also possible.

AMBERG, Detroit.

Nose

POSTERIOR SINUSITIS AND ITS OCULAR COMPLICATIONS. G. CANUYT, J. RAMADIER and VELTER, Ann. d. mal. de l'oreille, du larynx **44**:39-81 and 140-178 (Jan.-Feb.) 1925.

By posterior sinusitis is meant inflammation of the sphenoid sinus and the posterior ethmoid cells. In this report are eliminated cases of cancer, syphilis, tuberculosis, mycosis, osteomyelitis and the group of classic, definite, suppurative sinusitis. The authors wish to confine their report to what they describe as latent sinusitis. They speak of the number of classifications which are used in this particular group (unrecognized sinusitis, latent sinusitis, sinusitis without pus, sinusitis without sinusitis).

In reality, there exists two groups of cases that are important to distinguish:

1. The first group, a complete examination leads to a probable diagnosis of sinusitis; and the second group, the most minute examination of the sinuses is negative and the surgical intervention itself does not affirm the existence of a lesion. In this class of cases, if the intervention is followed by cure or relief of the condition, it would seem to show the sinus etiology, or at least the good foundation of the therapeutic procedure.

The authors speak of the importance of knowing how to look for a latent sinusitis by methodical physical examination; knowing what symptoms should cause one to suspect the existence of a latent posterior sinusitis. These symptoms are ocular symptoms, painful symptoms and reflex symptoms (asthma and spasmodic coryza).

The ocular symptoms which result from latent posterior sinus disease are: (1) oculomotor troubles; (2) choroiditis and chorioretinitis; (3) visual disturbances from involvement of the optic nerve.

In speaking of the oculomotor disturbances, the authors state that the motor nerves of the eye can be involved by posterior sinus disease, but this involvement is much rarer than in the case of the optic nerve.

2. Choroiditis and chorioretinitis:

Up to the present time, these symptoms have been rarely reported as symptoms due to a sinusitis. Their progress under the influence of sinus treatments permits one to add them to the symptoms caused by latent sinus infection. Brandes has reported three cases of acute chorioretinitis of ethmoid origin. The aspect of the chorioretinal lesions was very special. The lesions were disseminated, round, yellowish, having evolved rapidly, some with complete resorption, others leaving a little discolored spot with a little mass of pigment in its center. Duverger and Lempert have reported an analogous case in which the limited lesions of acute chorioretinitis evolved rapidly after curettage of the ethmoid. Coppez also cites many cases seen of choroiditis from sinusitis.

Dupuy-Dutemps has cast some doubt on the reality and the frequency of this etiology, and without denying absolutely the possible rôle of chronic sinus infection in the appearance of a chorioretinitis, he estimates that the proof is lacking in the majority of observations. One question is raised: Do there exist clinical characteristics which could permit the differentiation of the lesions of chorioretinitis of sinus origin from other forms of disseminated chorioretinitis? And the authors answer this question by stating that there appear to be no distinctive signs; however, the lesions seem more limited, less confluent, more discrete and leave after them little or no pigment.

3. Visual disturbances from involvement of the optic nerve:

Two forms of visual disturbances are described: (1) optic neuritis; and (2) retrobulbar optic neuritis.

Sometimes these cannot be sharply separated, and there are intermediate forms which prove that certain of these optic nerve lesions have not the independence which are at times attributed to them.

According to the authors, optic neuritis, properly speaking, is characterized essentially by papillary change. The vascular changes are constant, venous hyperemia, often very intense, dilatation and tortuosity of the veins, diminution of the caliber of the arteries, less marked at the onset, more accentuated later. The picture of the papilla often varies. Most often, one notes either a hemorrhagic papillitis or an edematous papillitis, but the latter much more rarely.

In many cases, and this fact appears important to the authors, the lowering of visual acuity is made by jumps, at times followed by slight improvement, but each shock leaves a persistent diminution of visual acuity after it. The long duration of this form of neuritis, the slowness of the progress of the lesions in the cases at hand have often been noted and contrast singularly with the habitual rapid progress of the infectious neuritis but reservations must be made on this point, for some cases of rapid blindness have been reported, and it is clinically impossible in the presence of an optic neuritis to say what will be its ulterior outcome; always the gravity of the neuritis must be held in mind, not only for the prognosis but for the determination of operative intervention.

Modifications of the visual field are constant; peripheral contraction is more or less regular at first, then gaps or notches in irregular bands or in sectors with dyschromatopsia more or less complete. In many cases the same changes occurring rapidly are reported, and as the lesions increase progressively, the visual field is gradually lost. At this time postneuritic atrophy has replaced the optic neuritis. The lesions cannot be remedied, and even in the case in which the sinus etiology is established and operation is decided on, cure is no longer possible.

Retrobulbar Optic Neuritis.—Here the ophthalmic signs are nil, at least at the beginning, and only functional signs exist. Above all, these consist of a considerable lowering of the visual acuity due to the appearance of a central scotoma.

The classic clinical picture of retrobulbar neuritis can be pictured as sudden onset with ocular and retro-ocular pains, rapid lowering (and often in several hours) of the central vision, ordinarily an absolute central scotoma both for white and colors, more often a scotoma from 10 to 20 degrees but at times a giant scotoma from 30 to 35 degrees. At times, other changes in the visual field can be found. These are paracentral scotoma by enlargement of the blind spot, and a scotoma more extensive for colors than for white. Van der Hoeve considers it a sign of great importance, but other authors consider it a sign of beginning papillitis.

In many of the patients, the progress of the optic symptoms attributed to posterior sinusitis does not differ from that of the conditions of the optic nerve due to the causes habitually recognized. This seems true, especially in pure retrobulbar neuritis, which, classically at least, in a benign affection is cured completely in three weeks with return of visual acuity to normal, and the persistence in the majority of cases of a slight papillary pallor. It is precisely this notion which certain authors have raised to an absolute dogma, and which has caused therapeutic results obtained by operation to be regarded as more or less coincidences.

The authors feel that certain restrictions must be laid on this dogma; all ophthalmologists have seen cases, rare it is true, but definite and very impressive, in which typical retrobulbar neuritis changes, at the end of a certain time, toward optic atrophy and blindness. Besides, intermediate cases show that it is difficult to affirm if one is dealing with a typical retrobulbar neuritis or with a neuritis susceptible to increasing progressively and going on toward optic atrophy. The authors feel it is not perhaps logical nor prudent in these conditions if the sinus etiology does not appear evident, to fold one's arms and wait until the retrobulbar neuritis heals itself alone.

In the heading of "Frequency of complications affecting the optic nerve," the authors feel that percentages have been differently interpreted by various authors, since the existence of retrobulbar neuritis of nasal origin is disputed by many. It is not to be doubted, however, that a sinus etiology exists in a certain number of the cases; either this is proved by real clinical signs of sinusitis or has been shown by exclusion of all other possible pathologic causes, and especially by the results of the sinus treatment after the defeat of all other means of treatment. Authors are far from being in agreement on this question.

In reality, it is very difficult to fix an exact percentage of the complications of this kind, since in many of the cases the sinusitis itself is doubtful and the visual complications are rare in comparison to the frequency of nasal suppuration, and for this reason they are even rarer in cases of latent sinusitis.

Morax, Chaillons and Kalt deny a sinus etiology, and they refuse to see in the published cases any demonstrative facts. To these authors retrobulbar optic neuritis appears to be a special infection which has a peculiar course, which cures itself spontaneously and completely and the cases cured by operation are only coincident. The authors feel that, in spite of the authority which is attached to the names of these observers, it is difficult to admit their opinion without restrictions.

According to our authors, retrobulbar neuritis is a localized neuritis, is less severe in prognosis than a neuritis with papillitis, and this particular localization makes one suspect the existence of a local lesion in the neighborhood and that thus the nature even of the condition limits the field of etiologic study.

Diagnosis.—In regard to the diagnosis, these authors state that the ocular symptoms of latent sinusitis differ very notably from those resulting from suppurative sinusitis. In the latter cases, most often there is a direct spread of the sinus infection to the orbit and its contents, giving rise to simple orbital cellulitis, phlegmon of the orbit, ocular paralysis of rapid course, optic neuritis of sharp progress with papillitis and other extensive inflammatory lesions in the fundus and finally venous thrombosis. Orbital cellulitis is very rarely shown in latent sinusitis.

Ocular complications in the form of rapid and early changes often primary in the optic nerve, the most evident clinical form of which is neuritis with

stasis, are signs of great value in the early diagnosis of a posterior sinusitis especially of a sphenoiditis. In other cases it is not a question of frank optic neuritis and papillitis, but of retrobulbar optic neuritis. Cases with oculomotor paralysis are rare, also cases with lesions of iridocyclitis, chorioretinitis, retinal detachment and hyalitis.

The authors formulate certain rules necessary for the conduct of a rational etiologic diagnosis:

1. A minute study of every general infection with particular reference for syphilis; and a search for and elimination of toxic causes such as tobacco and alcohol (the latter is not as likely as some would think).

2. Very complete neurologic examination, particularly for multiple sclerosis.

The existence of retrobulbar neuritis in multiple sclerosis cannot be denied, but its frequency and importance should not be exaggerated; it must be recalled that in a considerable proportion of cases neither syphilis nor a neurologic condition are etiologic factors; among these cases there perhaps are some resulting from sinus infection.

In the interpretation of postoperative cures, those authors who have admitted the sinus etiology have been reproached for not bringing anatomic proofs and sufficient operative reports to base their opinion on the cure following operation, which, others say, is not to be surprised at since slight papillitis (and especially retrobulbar neuritis) heals spontaneously. Certainly the interpretation of the therapeutic rôle in an intervention is difficult to make, especially in the frequent cases in which no visible sinus lesion is revealed, and in those in which an ordinary simple intervention has caused improvement or cure. Cases, however, are numerous in which the observations offer all the desired clinical proofs, when all the etiologic points and diagnosis have been successively searched for and studied, when the tests of specific treatments have been made, and when intervention only on the sinuses has been followed by improvement. Very often this rapid improvement has been obtained in old cases, the duration of which had greatly exceeded the usual duration of optic neuritis. It appears quite difficult then to refuse to employ any useful therapeutic action when all other forms of treatment have failed and one believes that a sinus infection, latent or weakened, is the only thing which can be the cause. If, in view of the ocular signs, the clinical examination confirms or renders possible a hypothesis of the sinus etiology, intervention must be done. On the contrary, after failure of other treatments and in the presence of a grave menace, intervention can be done by simple means at first and by more extensive means later, if the first failed. This will give the patient a greater chance of cure than following the expectant treatment.

There are three anatomic-pathologic lesions of macroscopic nature: (1) closed empyema; (2) sinusitis from common ordinary lesions; (3) hypertrophic sinusitis.

With closed empyema, the suppuration cannot escape and three outcomes are possible: (1) the inflammation recedes and the secretion is absorbed; (2) the secretion continues up to a certain point but remains latent, hidden, although being capable of presenting intermittent discharges; (3) the secretion continues, causing a dilatation of the cell, which can attain enormous proportions and finally ends by rupturing, and this transforms a closed empyema into one that is open.

Acute sinusitis attacks more or less a number of the sinus cavities; most heal, only a few pass to the state of chronic infection on account of the special disposition of their ostia.

In regard to sinusitis from ordinary slight lesions, every sinus infection does not necessarily give birth to an abundant suppuration. There exist infectious lesions of feeble degree, causing only slight changes and a very discrete catarrhal and mucopurulent secretion. They can remain quiet and so they cause only slight inflammatory lesions in the nasal mucosa. Because of certain special anatomic conditions, these slight infections are not less likely to cause severe complications when it is a question of a sinus surrounded by important structures as are the posterior sinuses. The operative findings show in these cases either a congested or edematous state or a granular degeneration or slightly myxomatous degeneration of the mucosa. At times, some mucopurulent secretions are recovered.

In regard to hypertrophic sinusitis, the authors state that under this term is understood an anatomic process, characterized by overgrowths macroscopically visible. These overgrowths are masses filling the paranasal cavities. At times, they have the appearance of an ordinary polyp of the nasal fossa. More often they have a different aspect of darker, reddish, nontranslucent, firm consistency with slightly irregular surfaces. In advanced cases they appear to enlarge the cellular cavities, breaking down the septum, breaking down even in mass the internal wall of the ethmoid. If one judges all the dimensions which certain of these new formations acquire, they can reach the size of a large kidney bean. One obtains the impression that they have destroyed certain cellular partitions in reaching such a size. This hypertrophic sinusitis appears to affect the ethmoid more easily than the other sinuses, but it is not limited to anterior posterior ethmoids. The lesions can remain strictly intersinus, but they also can extend beyond the sinus limits under the form of either a mucous polypi discrete in the nasal fossa, or by hypertrophic degeneration of the head or tail of the middle turbinate.

From the histologic point of view, these new formations are essentially not to be distinguished from polypi of the nasal fossae. Histologically, edematous infiltration distending in the capillary meshwork of the submucous connective tissue are shown. Zones of leukocytic infiltration mark a certain degree of inflammation, and at times a relative abundance of eosinophiles; but the latter elements are found also in the ordinary mucous polyp of the nasal fossa. In many subjects examined histologically, the underlying bone has appeared practically normal. However, certain authors have reported bony histologic lesions such as hypertrophy of the periosteum with fibrous degeneration and osteoblasts and osteoclasts.

For a long time, Sluder has insisted on these bony changes which he describes as hyperplastic sinusitis. The authors feel that Woakes theory, namely, that the hyperplastic lesions of the mucosa follow primarily the bony necrosis, cannot be held. They feel that the bony changes are secondary to the degenerative changes in the mucous membrane.

The histologic lesions found in cases in which no macroscopic alteration could be found consist of: (1) changes in the mucosa; sometimes an ordinary inflammatory process devoid of all interest; (2) hypersecretion of the mucus, characterized by very marked congestion of the superficial calciform cells; (3) no apparent lesion of the epithelium, but edematous inflammatory infiltration with sclerosis and thickening of the mucosa. In some complex lesions, microscopic findings by the authors are: (1) mucous hypersecretion of the epithelium and nearby glands with sclerosis of the chorion; (2) metaplasia describing pavement epithelium; edematous infiltration or sclerosis; (3) folded aspect of the superficial epithelium; (4) the presence of a calcified ring with concentric layers of an unknown significance.

In their summary on histologic studies, the authors state that when retrobulbar optic neuritis is concerned, the finding of a macroscopic sinusitis is rare, but microscopic alterations are frequent and there are cases in which all examinations are negative.

In discussing the etiology and pathogenesis of latent posterior sinusitis, the authors state that it is reasonable to believe that many sinus conditions pass unrecognized, as one must admit that sphenoidal sinusitis has frequently been found at necropsy and clinically rarely diagnosed. It is certain that rhinologists, on the whole, should put into operation anything to remedy this tendency to overlook posterior sinusitis. The authors ask: Why do the posterior sinuses remain overlooked? They feel that not only are the posterior sinuses frequently involved, but that frequently acute infections of the sinuses which apparently clear up, really disappear into the posterior sinuses, in which they tend to become chronic. The causes favoring latent posterior sinusitis are chiefly anatomic factors which favor stagnation and faulty drainage.

Most authors consider infection only an accessory factor in the production of latent sinusitis, other factors being changes in the circulation secondary to certain anatomic abnormalities, endocrine disturbances and changes in nutrition due to circulatory changes. The anatomic conditions favoring posterior sinusitis are realized in the large sinuses, as any infection in the large sinuses encroaching as they do on the nearby regions, can cause the complications under discussion. The authors feel that these favoring conditions being admitted, the different mechanisms which can explain the complications secondary to posterior sinusitis are toxic, infectious propagation, circulatory disturbances and compression.

The authors have insisted on the existence of venous anastomosis between the veins of the sphenoidal sinus and the ophthalmic venous system on the one hand, and between the sphenoidal sinus network and the vessels of the sheath of the optic nerve on the other hand. They feel that the existence and constancy of the central posterior vein of Kühnt and Vossius, situated as it is in contact with the macular bundle and the canalicular course of the optic nerve in the very center of the nerve, is of great importance in transmitting microbic toxine to the papillomacular bundle.

In regard to circulatory disturbances, the authors feel that simple congested phenomenon can be of first importance in the pathogenesis of the symptoms under discussion. In regard to compression, there is no doubt but that this is a factor to be considered.

Canuyt, Ramadier and Velter feel that the vascular theory is the one which accords best with the majority of known facts. It is quite difficult to tell the respective rôles which it must play, either in direct propagation of toxic infection from the sinus mucosa to the optic nerve by the venous route, or by local circulatory disturbances purely congestive in relation with the same changes in the mucosa of the posterior sinuses.

In regard to examination of the posterior sinuses, the authors feel that a very careful and repeated examination must be made, making use of all possible methods of examination such as anterior, middle and posterior rhinoscopy, nasal pharyngoscopy, thorough shrinking of the nasal mucosa by cocaine-epinephrine, catheterization of the sphenoid orifices and roentgen rays. They state that rapid and superficial examinations must be abandoned, and that the following regions of the nose must be thoroughly investigated: (*a*) the olfactory fissure; (*b*) posterior part of the middle turbinate and the nearby turbinates; (*c*) sphenoethmoid recess and the anterior wall of the sphenoid;

(*d*) the choanal arc. The changes to be looked for are the presence of any secretion, hypertrophic changes in the mucosa and discrete polypi. The authors give their method of examination in great detail.

Endonasal Therapeutics.—In regard to treatment, the authors advise endonasal treatment (extrasinus), cocaine-epinephrine, slight surgical intervention on the middle or inferior turbinate, septum, spurs, etc., and adenoids, and direct sinus intervention. The operation they advise is a direct spheno-ethmoid operation. They feel that the endoseptum route of Hirsch and Segura, though it gives a complete view of the sphenoid, is not suitable for operations on the posterior ethmoids. They favor the endonasal route, reserving the external route for grave suppurative sinus conditions. They feel that the old conditions are not favorable for operative success, but there exist some, nevertheless, in which cure has been obtained.

Their conclusions are that a retrobulbar optic neuritis having been diagnosed, its origin remaining unknown in spite of all examinations; rhinologic and roentgen-ray examinations revealing no definite appreciable lesions, the conduct to follow as it appears to them is as follows: Intensive specific treatment for eight days associated with rest and local nasal treatments, that is, cocaine-epinephrine, inhalants, etc. In case of failure, practice either the sphenoid puncture or resection of the middle turbinate, etc. If there is no improvement in two or three days, then resort to sinus surgery. Some conditions, by the rapidity of their course, force one to a prompt sinus operation. It is not a trivial matter to lose twenty-four to forty-eight hours in the presence of a malady the progress of which is very rapid, and to neglect the chances of success by even partial intervention. The opthalmologist carries the responsibility of making the diagnosis of the operative indication. His duty is to search attentively to eliminate or retain all possible etiologies of the eye conditions. It is he who must demand and call for the operation. The rhinologist carries the responsibility of the surgical intervention, but he ought to intervene only after being assured that all examinations have been systematically and rigorously practiced, for if the glory of success goes to him, the possible disaster will also be imputed to him.

In closing, the authors state that a method is judged by its results. At the present time it is difficult to make an exact and definite opinion on the subject under discussion. Time is necessary to settle this question. The authors state that "Let us not be, as someone has written recently, more Sluderistic than Sluder himself, but let us remember quite simply that for the greater good of the blind and the paralyzed, the opthalmologist and the rhinologist must lend aid and assistance."

PENETRATION INTO THE ORBITAL CAVITY DURING THE COURSE OF AN ETHMOIDECTOMY BY THE ENDONASAL ROUTE. HICGUET, Ann. d. mal. de l'oreille, du larynx, **44**:193-194 (Feb.) 1925.

Hicguet reported this case before a meeting of the Brussels Society of Oto-Rhino-Laryngology. It concerned a woman, aged 53, suffering from diffuse polypoid degeneration of the left ethmoid.

After the removal of the middle turbinate, the anterior ethmoid cells were cleaned with a Luc forceps, as the middle meatus was very narrow on account of a high deviation of the septum. At the first stroke the patient complained of a sharp pain in the eye on the same side, in spite of a careful local anesthetic. On seizing the polypoid masses in the region of the amputated head of the

middle turbinate with forceps, more ocular pain followed with the appearance of edema of the upper eyelid. The operation was stopped. That evening the patient presented ecchymosis of both eyelids.

The author attributed this result not to a fault in the operative technic, but to a malformation of the os planum in the internal part of the orbit, either an extreme thinness or an absence of the os planum so that the orbital periosteum will remain fixed to the nasal mucosa.

H. H. Vail, Cincinnati.

Pharynx

Aspects of the Precollagenic Reticulum in Normal and Pathologic Palatine Tonsils. Donato di Donato, Arch. ital. d. otol., rinol. e laringol. **36**: 812-817, 1925.

From his researches on the histologic structure of the precollagenic reticulum, in which, after experimenting with other procedures, he found the Bielschowsky method as modified by Levi to give the best results, di Donato reached these conclusions: Not only in the normal but also in the pathologic palatine tonsil the precollagenic tissue is always present in abundance. In the hypertrophic tonsil the "gitterfasern," or lattice fibers, are more numerous and thicker. In the tonsils, the origin of these formations is always perivascular. As for the cause of the greater thickness and the greater number of the "gitterfasern" observed in the hypertrophic tonsil, it is probable that these formations react to the same pathogenic influence as all the other elements of the lymph glands—the influence that occasions hyperplasia and hypertrophy of the tonsils as a whole.

Wolcott, Chicago.

Investigation Concerning Mastoiditis (Endostitis Mastoidea). Wilfried Krainz, Ztschr. f. Hals-, Nasen- u. Ohrenh. **13**:361 (Jan. 18) 1926.

Krainz divides his extensive article into ten parts: (1) introduction; (2) lining of the cells; (3) demolition of bone; (4) aplastic cases; (5) necrosis; (6) bone apposition; (7) Sharpey's fibers; (8) relative occurrences; (9) clinical considerations; (10) summary.

Krainz devotes over 100 pages to an exhaustive essay, which should be read in the original. He bases his original deductions on 100 cases viewed from a histologic standpoint. Chips procured during the operation were examined. Larger pieces of the cortex and of the tip, and smaller pieces of the more deeply situated parts in the region of the antrum were mostly studied. The pieces were conserved and hardened partly in a solution of formaldehyde, partly on 4 per cent formaldehyde solution. The pieces were decalcified according to Schaffner in 5 per cent nitric acid or, preferably, in a mixture of hydrochloric acid and sodium chloride according to v. Ebner. They were embedded in celloidin. Some specimens were incompletely decalcified according to Pommer in the solution of formaldehyde, and frozen cuts were made. The celloidin cuts, from 4 to 6 μ thick, were usually stained with iron hematoxylin and eosin, either according to Hansen, Delafield or Weigert, sometimes after the methods of van Gieson or Mallory; some were stained with aniline. They were embedded in Canada balsam or in glycerine. Five hundred specimens were made the basis of the histologic deductions.

TUBERCULOMA OF THE MIDDLE NASAL MEATUS. W. TONNDORF, Ztschr. f. Hals-, Nasen- u. Ohrenh. **13**:466 (Jan. 18) 1926.

Tuberculous disease processes in the nose are found primarily at the nasal septum, then at the floor of the nose and the lower turbinates. Only in rare cases is the process confined to the middle turbinate or to an accessory cavity. In the literature, only single analogous cases are reported by Bernd, Guyot, Marcelli, Pasch, Suchannek, Torrini, perhaps also by Bronner, Brown-Kelly and Weil. All emphasize the rarity of the occurrence. The patient in question, a woman, aged 49, was sent to the clinic by a specialist who reported that he had removed a specimen from the left nostril, which resembled sarcoma. The patient, as well as her sister, suffered from ozena since they were 10 years old. A year ago following "influenza," much pus was secreted from the left nostril, which became obstructed. A specialist removed part of a tumor from the nostril. Each manipulation, even a simple examination, was accompanied by profuse bleeding. Tonndorf found a tumor in the left nostril which was covered on its red raspberrylike surface with crusts, and bled easily when touched. A tumor, the size of a hen's egg, was removed. The peduncle was located under the middle turbinate. The histologic examination showed a fibroma covered with stratified squamous epithelium. In its marginal zone, numerous tubercles were present, which contained numerous giant cells. These tubercles showed partly caseous degeneration. No history of tuberculosis could be found. On account of the possibility that the tumor originated from the maxillary antrum or the ethmoid cells, these cavities were opened. The maxillary antrum was small and formed a common cavity with ethmoid cells. The mucous membrane was examined histologically. It did not show any signs of tuberculosis. The necessity of removing a piece for microscopic examination is obvious. Guyot, Katz, Koschier, Manasse, Rockenbach, Onodi, Perrier (case, Coenen), have reported cases in which malignant tumors were assumed to have been present when, in reality, the tumor was a tuberculoma.

CONDUCTION ANESTHESIA OF THE MAXILLARY NERVE. REDDINGIUS, Ztschr. f. Hals-, Nasen- u. Ohrenh. **13**:470 (Jan. 18) 1926.

The method was proposed first by Carrea, Buenos Aires, and was used independently by Hofer, Vienna, and Fischer, Hamburg. The ganglion sphenopalatinum is injected through the canalis pterygopalatinus. The foramen rotundum lies at a distance of about 3.5 cm. from the foramen palatinum, therefore the needle must be introduced to a corresponding length. The foramen palatinum is found at the posterior border of the hard palate next to the last molar, in which the alveolar process turns to the horizontal part of the palate. The mucous membrane usually shows a small sinking in at this spot. It becomes more visible when tincture of iodine is used for disinfection. The oral cavity is cleaned with hydrogen peroxide, then iodine is applied to the palate. The mouth is opened wide; the syringe is held in the direction of the middle incisors. When sure that the channel is entered, the syringe is pushed forward slowly for 2 cm. The channel directs the way. With moderate pressure, about 4 cc. of a solution of 2 per cent procaine is injected. Some epinephrine solution may be added if desired. Reddingius used the method when performing the Luc-Cadwell operation. Hubmann reported 250 successful injections.

AMBERG, Detroit.

Miscellaneous

ILLUSTRATIVE CONTRIBUTION TO SENSORY APHASIA IN OTOGENOUS EXTRADURAL ABSCESS IN THE LEFT MIDDLE CRANIAL FOSSA. E. BUECH, Ztschr. f. Hals-, Nasen- u. Ohrenh. **13**:351 (Jan. 18) 1926.

Buech reports a similar case to that of Thormann (volume 2 of the same publication). Anamnesis and findings pointed with the greatest probability to an abscess of the brain. Amnestic aphasia and paraphasia were present, but no paralysis of the oculomotor nerve. Although an abscess of the brain was not found during the operation, its presence could not be excluded with certainty. Only the further course showed that an abscess was not present. This was shown by the continued improvement and the receding prolapse of the brain. The aphasic disturbances also disappeared, although rests of the same could be observed five months later. Therefore the patient had suffered from an otogenous extradural abscess with circumscribed encephalitis. Voss has seen cases in which a nonsuppurative acute encephalitis was observed in connection with a purulent otitis.

AMBERG, Detroit.

Society Transactions

CHICAGO LARYNGOLOGICAL AND OTOLOGICAL SOCIETY

Jan. 4, 1926

HARRY L. POLLOCK, M.D., *in the Chair*

PRELIMINARY REPORT ON EPHEDRINE. Presented by DR. GEORGE F. FISKE.

Most of you have seen Dr. George Fetterolf's report on ephedrine sulphate in the August number of the *Archives of Otolaryngology*. Dr. Fetterolf was so kind as to help me to obtain a small supply of both the chloride and the sulphate, and this is a short report of its effects on the nasal mucous membrane.

It was used on twelve persons, including myself. The solutions were 2 and 1 per cent, and 1:500. The most satisfactory and least irritating method of application seems to be a cotton pledget, rolled and saturated with the solution and then introduced into the lower meatus and left for two to three minutes in contact with the mucosa. With the 1 and 2 per cent solutions the shrinkage began immediately and was complete within two to four minutes. The contraction remained complete for from one half to two hours, the relaxation coming on more quickly in cases of acute rhinitis. The solution 1:500 caused a marked shrinkage, but not complete enough for operative purposes. In several cases the 2 per cent solution was used in connection with a 4 per cent solution of cocaine, both separately and with a mixture—half and half—of the two solutions, producing the effect of both. No irritation was observed and no after effects, either good or bad. The action as regards shrinkage of the mucosa was very like the 1:1,000 solution of epinephrine chloride, except that the paleness produced was less marked.

The aqueous solution seems to resemble the sulphate of atropine solution in its stability, which is of marked advantage. Its field of usefulness would seem to me to lie in intranasal operating. The alkaloid itself I have not obtained as yet, though I hope to. Both the chloride and the sulphate crystals are easily soluble in water. The price quoted me from Philadelphia was $1.50 per gram. The supply at present is limited, which is certainly understandable, if the plant *Ephedra vulgaris* must be brought from China.

I had hoped to have a larger supply in order to give it to all members of this society who are interested, but though I have ordered some from Dr. Read in Peking, and also from France, it has not as yet arrived. When it does, I shall be glad to divide with you. It will then be tested with novocaine for local anesthesia. While the expense at present is very great, there are some of us who remember paying $1.00 per grain for cocaine.

DISCUSSION

DR. JOSEPH C. BECK said that Dr. Fiske was kind enough to let him have two small bottles of the solution, but after using it for two or three weeks Dr. Fiske wrote him that the solution had not the strength that he thought it had, for it was less than 2 per cent. Dr. Beck employed it in application as well as spray form and in this weak solution there was some shrinkage of the nasal mucosa. He had not observed any reaction, such as sneezing, which occurs

following the use of epinephrine. He believed it would be a satisfactory solution when perfected and an aid to therapeusis.

Dr. Otto Stein thanked Dr. Fiske for the supply of the solution which he had placed at his disposal. He had applied it with a dropper, placing 2 or 3 drops of a 1 per cent solution in the nostrils, with the same effect Dr. Fiske mentioned. There had been no complaint on the part of the patients. He found the contraction very suitable with 2 drops in each nostril, and thought it was ample for all purposes, used either with a weak solution of cocaine or alone. He had not studied the lasting effect, but had used it routinely in most of his patients. The contraction occurred immediately, and evidently remained for some time. He considered ephedrine a wonderful addition to the therapeusis for local application, and could not see the need of a 5 per cent solution when a 1 per cent acted so satisfactorily.

Dr. A. A. Hayden stated that he had used ephedrine in a 1 per cent solution, and found the contraction and blanching of the mucous membrane was quite as prompt as with the oily solution 1:1,000 or epinephrine. He had not used it in operative work but in the office. He tried it in his own nose and thought the contraction lasted for two or three hours. The advantages of the solution he believed to be as stated by Dr. Fiske, and considered it of great value.

Dr. Frank Novak, Jr., asked if anything was known concerning the toxicity of the drug.

Dr. Joseph C. Beck said that Dr. Fetterolf of Philadelphia told him the laboratory was working this out at present and that information would soon be available.

Dr. George F. Fiske said that a report in the *Journal of Pharmacology and Experimental Therapy* by Dr. Chen, stated that it had been used in shock and that there was no toxicity at all.

Congenital Osseous Atresia of the Posterior Nares. Case Report: Entrance Thesis. Presented by Dr. Jesse H. Roth, Kankakee. (Abstract.)

The case reported was that of a girl, aged 12, who was slightly anemic, and who gave a history of never having been able to breathe through the right side of the nose. Removal of adenoids in early childhood had given no relief. She had never been able to clear the right side of the nose of mucus, which at times caused a slight eczematous condition about the ala. There was no asymmetry of the face and the palate was only slightly higher than normal. Examination showed the right side of the nose filled with glairy white mucus, which was removed by lavage. The turbinals were slightly atrophic and the mucous membrane paler than on the left side of the nose. It was impossible to use a postnasal mirror, for a complete bony obstruction filled the posterior part of the choana, probably situated at the posterior border of the hard palate. The plate extended from the floor of the nose and the septum outward to the lateral wall and backward to the sphenoid. About midway up and close to the septum was a small canal that would admit a probe. This canal extended toward the septum but ended in a blind pocket. Firm resistance was met in every part of the obstruction. The parents refused to submit the child to operation, and further investigation was impossible.

DISCUSSION

Dr. W. E. Grove (Milwaukee, Wis.), thought the difficulties in handling these cases were not the operative procedures, although these were sometimes difficult because of the age of the patient, but the difficulty in keeping the

opening from closing. Many different methods of doing this have been suggested. He mentioned an interesting article which appeared in the *Acta-oto-laryngologica* several months ago in which the authors, Bourgeois and Poyet, advised making the opening through the atresia by whatever method one wished, and then allowing the secondary membrane to close the opening again, which it will do almost completely if left alone. After this had taken place, they then employed electrocoagulation of the membrane and reported some excellent results. Dr. Grove had operated on a patient of this sort, a woman, aged 42, who consulted him because of difficulty in hearing. He had no trouble in keeping the opening patent and made his approach through the posterior portion of the septum.

While studying his case, it occurred to him that a nose which was obstructed in this fashion would be ideal ground for sinus infection, and on making roentgenograms he found practically all the sinuses on that side of the head were much blurred, but on opening the antrum found only the presence of a heavy, glairy mucus. Dean had called attention to the presence of sinus infection in all the children he had seen, with congenital bony obstruction of the choana.

Vogel recently called attention to the coexistence of this condition with various congenital anomalies of the face, such as fistulas, misformed alae, unilateral sweating and the like.

Dr. J. Holinger said the occlusion of the choanae was more a question of degree than of straight pathology, as all transitions exist, from wide open to a very narrow, and to the completely closed choana. The closed choana gives the most symptoms; but often mouth-breathing is due to one congenitally narrowed. He thought the small choana was more frequent than is generally diagnosed or suspected. He knew of four cases of complete occlusion of both choana. In new-born or in small babies he would hesitate before he filled the nose with water, for if there is a small opening the water is likely to run down into the windpipe and make trouble. A safer means of diagnosis is the use of the Politzer method, without closing the other nostril. The child will cry, and under normal conditions air and mucus will come out of the open nostril. If this does not occur there is indication of occlusion.

He agreed with Dr. Roth and Dr. Grove that it is very difficult to keep the opening in the choana patulous after operation. Such a condition must be watched for a long time. As soon as granulations form, they must be cauterized. As a rule, persistent treatment will establish a permanent opening.

Dr. Elmer L. Kenyon said that he treated such a condition several years ago in a girl, aged 16 or 17. The closure was on the left side, and she had a decidedly deflected septum with a marked curvature toward the opposite side. He opened the bony wall with a trephine and the patient breathed comfortably. He enlarged the opening with a burr a few weeks afterward, but he did not know the subsequent history of the case.

Dr. Austin A. Hayden thought there was always a considerable amount of danger present in attempting to force water or air into a nostril which is suspected of being closed at the posterior portion. The air, water or mucus can be forced out through the tear sac, and a diagnosis made in that way; but at the same time the eustachian tube is quite as apt to receive the forced fluid and this is likely to set up acute otitis. He believed the inability to pass a catheter or tube from the nose back into the antrum would answer just as well as a means of diagnosis. He had never seen complete occlusion even of

one side, or at least had not recognized it. It might have been that some of the "blue babies" who had died at the hospital had died from this cause. It seemed to him that it might be well for otolaryngologists to interest themselves in this question, with the idea of securing some postmortem examinations on these children, or at least a digital examination of the nasal pharynx of any child who died of such a respiratory disorder. The determination of the degree of patency seemed to him very important. In looking at the front of the nose, the septum and turbinates, if deformed, often are straightened out or removed, but this does no good if there is a narrowing behind, and the patient will still have the symptoms for which he sought relief. Dr. Hayden had seen quite a number of posterior openings that differed greatly in size on either side, and not a few cases of obstructed breathing had been explained to him and to the patients in that way, so that the patients would understand why the operation was not attended with all the good results they had anticipated.

Dr. Joseph C. Beck called attention to the paper of Dr. Lebensohn of two years ago, and said that at that time in the discussion he mentioned their experience in a few cases from the diagnostic and therapeutic viewpoint. The roentgenogram had not been mentioned by anyone in the present discussion, but it is of great assistance in the diagnosis. In the treatment, everyone has the same difficulty in keeping the opening patent because of the cicatrization, but in one case, in a boy, aged 7 years, good results were obtained by passing a catheter through the nose after the opening was established, and then bringing back a metal tube which was held in front and tied by means of a string through the opposite nostril. This was kept in place until complete epithelization occurred (about six weeks) and the opening remained patent. Dr. Beck thought it was not necessary to have a child old enough to permit putting the finger in the postnasal space, for any instrument held against the posterior wall of the pharynx, similar to an adenoid curet, only solid, would enable one to use a burr without injury to the posterior wall of the pharynx.

Dr. C. F. Yerger asked whether the nasopharyngoscope would not be of advantage in these cases. He thought it could be used through the opposite nostril with good results.

Dr. Jesse H. Roth stated that since his paper was written, three or four reports had appeared in the literature. They now had another patient under observation who had had an operation performed for congenital osseus atresia, but the opening had closed over. In that case the roentgenogram showed that the closure was intact. He knew of no means to facilitate the diagnosis aside from those that had been reported, and filling the nose with water was one of the means of diagnosis recommended.

The Theories of Hearing. Presented by Dr. J. Holinger. (Abstract.)

The theories of hearing are neither so clear, nor do they explain all the phenomena so well, that we should ignore all attempts at anything better. Specht has described the great changes that the study of the soundbox has brought about. Edison used it in the phonograph and in the radio. Its laws must be valid in the middle ear. The sound waves produce changes of pressure in the middle ear which are transmitted by the membrane of the round window to the labyrinthine fluid. The stirrup and ossicles act as a brace. The changes of pressure in the fluid become the irritants for the hearing cells.

Specht thinks that in hearing by bone conduction, the vibrations of the bone are transformed directly into changes of pressure in the fluid of the labyrinth. He does not recognize the physical impossibility of that. He, furthermore, overlooked the works of Siebenmann's assistants, who proved that Corti's membrane has a very important function in the process of hearing. Finally, why should the drumhead and the chain of ossicles act as a brace? They are under the same changes of pressure as the membrane of the round window. Dr. Holinger thought it quite feasible to accept Specht's theory and combine it with Bezold's theory of the function of the chain of ossicles.

DISCUSSION

Dr. Alfred Lewy said that according to his understanding of Dr. Holinger's presentation of Specht's theory, it resembled very much the theory of Pohlman of St. Louis, which was, briefly, that the drum membrane and chain of ossicles acted as a damper on the sound waves which entered both by air and by bone. Recently, Fowler published an article on bone conduction, in which he called attention to the fact that there is no such thing as purely air conduction or purely bone conduction. An impulse given to the bones of the skull is also partially transmitted through the air in the external canal via the middle ear to the fluid of the labyrinth as well as directly through the bone, while impulses arriving through the air are also partially carried through the bone, so that the terms air conduction and bone conduction are really relative terms.

The question raised as to how the sounds transmitted through the drum membrane and middle ear can enter at the oval window to the exclusion of air vibrations transmitted directly across the tympanic cavity to the membrane of the round window was perhaps best answered by Bezold's investigations (quoted by Edelman). The area of the membrani tympani multiplied by its excursion distance is to the product of the area of the foot plate of the stapes multiplied by its excursion distance as 778 is to 1; therefore, impulses transmitted from the membrani tympani through the leverage system of the chain of ossicles are increased 778 times in intensity when delivered to the fluid of the labyrinth at the oval window. Whatever air waves reach the membrane of the round window across the tympanic cavity are not increased in intensity by any such leverage system, and must be very low in power compared with that exerted at the oval window. It thus seemed that Bezold's theory that the elasticity of the round window membrane merely permits movement of the nonelastic fluid of the labyrinth under the impulses delivered at the oval window. Edelman also called attention to the fact that the relation of the specific gravity of water to that of air is 774 to 1, approximately the leverage relation of the movement of the membrani tympani to the movement transmitted at the oval window, and that it is very improbable that this significant relation is a mere coincidence.

Dr. Robert Sonnenschein said that the ratio of 700 to 1 was beautifully shown in a series of articles collected by Edelman, so that one could see that ratio of the drum membrane compared with the stapes. It seemed to Dr. Sonnenschein that one of the principal objections to the acceptance of the theory of Specht was that the oval window and the drum membrane, with the stapes, acts merely as a brace. When a number of sounds are produced, only one curve results because a membrane can only react in one direction at a time. It is well known that the low tones have a marked amplitude of excursion, and very little intensity, and it takes the lever action of the ossicular chain to transform these into tones of smaller amplitude but greater intensity to permit them to be transmitted via the oval window. If there is loss of the proper mobility

of the ossicular chain the low tones are not well heard. He believed that Bezold's original theory still held.

Dr. Frank Novak, Jr., expressed his interest in the paper but found that he had some difficulty in following Dr. Holinger. This was probably due to the difficulty of keeping clearly in mind the basic physics of sound. Dr. Holinger spoke of the disturbance in the air and then the changes in the endolymph, and mentioned the fact that the waves became pressure waves in a fluid medium. This was a little confusing. Is not sound simply matter in rapid rhythmic motion? Whether this matter be in a gaseous, fluid or solid state does not not change the kind of energy. The type of energy is no different whether it is present in a fluid or in a gaseous medium. Another point which interested him was the effect of pressure on colloids, and he asked Dr. Holinger whether his statements were supported by any experimental work on colloids.

Dr. J. Holinger said there had been experiments that showed that any outside change of the cell has an influence on the concentration of colloids in the presence of ions. This is Specht's hypothesis, but Dr. Holinger did not agree with this, in view Siebenmann's experiments. Specht had not mentioned these experiments of over-irritating the labyrinth of birds. Yoshee, in his atlas, showed that the hearing cells farthest from the pivot of the membrana tectoria were the ones which were most destroyed, while the hearing cells close to the pivot were very little injured, or remained intact.

As to the lever action of the chain of ossicles, this was the point he brought against the theory of Specht. He believed the footplate of the stirrup did not act simply as a brace, but that it has an active function, and the form of the joint between the malleus and incus proves this. The formation of the joint of the incus with the little tooth on the side makes it impossible for the hammer to move inward without taking the anvil along, while the hammer can move outward without taking the anvil along. If the ossicles acted as a brace this mechanism could not be explained, while it fits accurately in the idea of the lever apparatus.

Dr. Holinger believed there was some good in the theory of Specht. Some points of it had to be changed considerably. Specht admits that Bezold was the most conscientious worker on the matter.

Dr. Robert Sonnenschein said that in air or other gases he believed sound waves were pressure waves and could easily be measured, but in fluids there could be very little compression. On the other hand, transmission of sound is least rapid in air, better in fluids and best in solids, but that referred only to the sound produced in that medium. If the sound passes from one medium to another, this does not obtain. If one produces a loud sound near a body of water the sound will not be transmitted rapidly or well. Perhaps this had some bearing on the fact that when going from the air into the fluid of the labyrinth, there is a change from one medium to another and it requires the action of the stapes in this transfer.

Dr. Holinger said that the passage of sound from air to water or from a solid body to water was a difficult question. He made this experiment many years ago while in swimming. He lay on the bottom of the lake in four feet of water while his friends made all kinds of noises, even shooting a revolver. He heard nothing at all while under water. In hearing by bone conduction, the transmission of sound waves from the walls of the labyrinth to the fluid of the labyrinth certainly does not change the pressure in the fluid.

Feb. 1, 1926

HARRY L. POLLOCK, M.D., *in the Chair*

CONGENITAL BONY OCCLUSION OF THE POSTERIOR CHOANA. Presented by DR. JESSE H. ROTH.

A woman, aged 35, came to the dispensary complaining of complete nasal obstruction and profuse mucopurulent discharge from the left side of the nose, which had been present since infancy. She gave a typical history of syphilis which had been contracted since marriage. She had received anti-syphilitic treatment and when presented the Wassermann reaction was negative.

There was a history of a nasal operation in an attempt to remove the obstruction six years before.

Examination showed the left side of the nose filled with mucopus. The mucous membrane was pale and glossy. It was impossible to pass an applicator into the pharynx, the resistance to the applicator being firm above but not below. The postnasal mirror showed complete obstruction of the left choana. There was malformation of the palate, especially on the left. The arch was well formed and not unusually high. The left maxillary sinus had been washed repeatedly and mucopurulent secretion was always obtained. The ethmoids were also involved.

DISCUSSION

DR. ROTH said they intended to investigate and see if the surgeon had removed the occlusion even with the floor. If not, they would use electro-coagulation and see if they could not get a good, smooth healing.

ATYPICAL FALSETTO VOICE. Presented by DR. ELMER L. KENYON.

The patient was a young man who gave a history of having a disturbed voice at 7 years. The classification had not been worked out. The concavity of the cords was attributed to paralysis either of the crycothyroid or the thyro-arytenoids, with a general disturbance involving the extrinsic musculature, which originates much oftener in the mental act of voice production than in local physical or functional disturbance. When the patient talked, the thyroid cartilage plunged quickly to the highest point attainable and stayed there quite constantly, under tension. The extrinsic muscles at the base of the tongue were likewise tense, making normal approximation of the vocal cords utterly impossible. Dr. Kenyon believed the disorder to be due to psychologic confusions with respect to voice production.

DISCUSSION

DR. J. HOLINGER stated that in singing the complete relaxation of the muscles of the pharynx is very important, and singing teachers long ago resorted to having the patient hum, or sing with the mouth closed. He thought this might help in Dr. Kenyon's case. If one taught the patient to hum, at the same time watching the neck and instructing him to relax completely, it might overcome the tenseness of the musculature.

DR. KENYON (closing) called attention to the cases reported by Dr. MaKuen a number of years ago, which were of much the same high pitched type as the one presented. In one of them the patient was instructed to talk in a low pitched voice, which he did. Following this, he did not return and the supposition was that he ever after talked with a normal voice. Dr. Kenyon believed that in the attempt that has been made to cure the high pitched voice in the past, errors have been made in thinking that the technic had been corrected. By using the imperfect technic of these persons, they can lower the

pitch considerably. The ear may be unable to decide whether the patient is using the normal or abnormal technic, unless one studies the extrinsic musculature. He felt practically sure that much more definite measures must be taken than those suggested by Dr. Holinger in order to secure the proper voice. He teaches the subject what his voice really is, then what the tone ought to be, and then how the extrinsic musculature acts normally. After the patient has learned to produce a voice with a normally acting extrinsic musculature, there is comparatively no difficulty, and the result invariably is a normal voice.

COMPLICATIONS OF EAR, NOSE AND THROAT OPERATIONS AND DISEASES. Presented by DR. JOSEPH C. BECK.

Case 1.—The patient, a woman, was presented because of the numerous operations she had undergone for the cure of mastoid infection. She had had five operations in a period of seven years. She gave a history of recurring attacks of dizziness, vertigo, headache and swelling in the region of the neck. There was nothing unusual in the examination of the canal except evidences of modifications of the radical mastoid operation and pus from the posterior part of the operated mastoid region. The ear stood out and the posterior part of the concha was very thick, as if it might contain an abscess. This condition of the concha had existed for two years. There was practically complete deafness present. The most interesting part of the case was the roentgenographic examination, which disclosed a large pneumaticized area with a large number of cells. A stereoscopic roentgenogram of the operated ear showed a number of cavities which might be interpreted as due to the previous operations or to unopened mastoid cells. Dr. Beck had recently operated on this patient. He had made an auricular incision at the junction with the mastoid process and another close to the hair line, bringing down a flap and exposing the whole mastoid area. This disclosed a large number of cavities which had been obscured, and which proved to be unopened mastoid cells which perhaps had been missed at the previous operations. Since this operation the patient had been free from trouble. (Three months afterward the patient had completely recovered.)

Case 2.—A man first consulted Dr. Beck on Jan. 4, 1926, because of defective hearing, soreness and ringing in the left ear which had been present for several months. There was no history of acute infection of the ear. There was frequent retention of wax in the ear, and at this time removal of the wax caused some soreness and swelling in the canal. There was almost complete stenosis and redness of the canal; not much involvement of the auricle. The hearing tests showed more reduction in the upper tone limit (audiograms were here presented). The patient's occupation was making steel pipes, in the process of which there was a great deal of noise and shaking. The diagnosis of nerve deafness was made. Examination of the canal showed an exostosis situated at about the center of the canal, which practically shut off the inner portion of the external canal. The roentgenogram showed the outline of the exostosis, but no evidence of clouding of the mastoid cells. He expected to perform an operation the following morning, and clear the canal of the exostosis by means of a retro-auricular incision.

Case 3.—A man, aged 43, entered the North Chicago Hospital with a history of having an acute edema of the larynx after being out hunting. He had had similar attacks before and had been hoarse for a number of years. He was in good health and had no complaint except loss of voice and difficulty in breathing during these attacks. Examination of the larynx showed a unilateral swelling on one side of the right cord; it appeared to be smooth and confined to one

side. There were no palpable glands in the neck. The man was very plethoric, and drank and smoked moderately. The Wassermann reaction of the blood was negative. Physical examination showed no evidence of any involvement of the lungs. A diagnosis of the neoplasm was attempted by suspension laryngoscopy, but they were unable to expose the larynx. They then resorted to the indirect method, but could not get near the larynx. They finally secured a piece, but not of sufficient size to permit a diagnosis. Following this procedure, the patient developed great difficulty in breathing and a tracheotomy was done the following day with difficulty. In doing this, no more than 1½ inches of trachea could be exposed on account of the patient's fat neck. The muscles of the neck were very large, and a large thyroid gland was encountered. After placing a large tracheal tube in the opening, packing was used to stop the oozing. The following day the man developed an infection around the tracheotomy which was very unpleasant. No definite diagnosis had been possible because of inability to secure tissue for biopsy, but this will follow. (Biopsy showed squamous cell carcinoma.)

Case 4.—This patient had had a radical mastoid operation several years before, which had nothing to do with his present illness. He came to the hospital with a boil on the nose, with edema of the eyes and a septic temperature. There was a hard lump over the cheek, but no evidence of sinus involvement. No incision or manipulation had been attempted, but the patient had been treated with a hot light over the face. This had given uniformly good results in similar cases.

These four cases were shown, as they illustrated the complications that arise in nose ,throat and ear diseases as well as in operations.

DISCUSSION

Dr. G. W. Boot, discussing the patient with the multiple mastoid operations, mentioned a patient, a nurse, who had had seven mastoid operations and wished to be operated on for a brain abscess, but there was no sign of such a growth. The patient had been sent to the country for a rest from hospitals and doctors.

In the tracheotomy cases he thought a sharp hook indispensable.

Dr. Samuel Salinger asked for an explanation of the edema or hyperplasia behind the ear in the mastoid case.

Dr. C. H. Long thought the mastoid case was important because Dr. Beck found the cells not previously opened by the other operators. He believed one should be more careful in searching out the mastoid cells in an effort to get successful results, and that thorough roentgenographic examination should always be made.

Dr. G. H. Mundt (by invitation), discussing the case of exostosis, said he was reminded of the case of a physician who came in with a history of not being able to hear in one ear with a stethoscope. Examination revealed swelling of the posterior superior wall in both ears. He made a diagnosis of exostosis, but advised the patient to have this confirmed by another otologist. This specialist made the same diagnosis, and as the patient wished to be operated on, he was referred to Dr. Beck, feeling that the exostosis was too near the middle ear to remove it with safety. Dr. Mundt asked Dr. Beck to tell of his experience with this case.

Dr. Beck (closing) agreed with Dr. Boot regarding the use of a hook in the tracheotomy cases, and said the difficulty in the case he reported was to

get down to the place in which one could put the hook. This could not be done because of the large amount of thyroid that was present.

He thought the cases with numerous mastoid operations were not uncommon, but that Dr. Long's point regarding the value of the roentgen-ray examination was good. In his case, when the tops of the cells which had not been opened in the sinus were removed, the cells were bluish and proved to be large, infected mastoid cells, a chronic infection of the lining membrane of the cells. He was not sure whether the results would be permanently good or not, for it was too soon after operation. Some types of cholesteatoma do not respond to any operation. The consistency of the swelling behind the ear was not that of cartilage, but of indurated inflammatory tissue. There was no marked thickness of the cartilage of the auricle. By taking a separate picture of the cartilage, they were able to differentiate it from inflammatory tissue.

In the case of nerve deafness, the patient had been given potassium iodide in small doses. The question was whether previous local treatment had had anything to do with it. This was an important question for this patient, for he claimed that following treatment of the external ear he became deaf. If this was merely nerve deafness, which had disappeared, it was a good point for his attorneys to fight over.

Dr. Beck said that, in many, exostosis occurs with fistulas, and Dr. Mundt's patient had an exostosis which bothered him a great deal. He attempted to remove it, but it was not located as well as in the case presented. It extended down to the middle ear and he did not remove any of it for fear of injuring the facial nerve.

This patient, who evidently had a carcinoma, was now ready for a laryngectomy, but from what they had learned doing the tracheotomy they would not do a laryngectomy either from above down or from below up, but would do a laryngofissure as soon as the condition was completely cleared up. This would be done by means of the new apparatus for electrocoagulation (radio knife), which would cut through all the tissues and seal them up against bleeding and implantation as it went along, for it cuts through cartilage as well as through soft tissues.

SINUSITIS WITH UNUSUAL POLYP FORMATION. Presented by DR. C. H. LONG.

The patient was a man, aged 37, who had had infection of the nasal sinuses for many years. This was thought to be so-called catarrh, and no attention was paid to it until he was accidentally hit over the ear by a fellow workman, which caused acute mastoiditis. When he sought medical aid for this condition, he was informed that his nose was filled with polyps and that they were probably the cause of the ear condition. The polyps were removed, but the ear condition grew worse. Another physician was consulted, and Dr. Long was called in consultation. A diagnosis of mastoiditis was made and a simple mastoid operation was performed. Following healing of this wound, the nose was examined and many polyps were found. A diagnosis of chronic double maxillary and ethmoid sinusitis was made, complicated by a badly deflected septum. At the time of this operation it was discovered that both sphenoids and the right frontal were also involved and these were cared for later. At the time of presentation, both of the maxillary sinuses were practically cleared up and apparently all the ethmoid cells had been evacuated and curetted. The anterior sphenoid walls had been punched out two or three times, but there was a tendency to reformation of the polyps.

UNUSUAL MASTOID REGION TUMOR. Presented by DR. H. L. POLLOCK.

The patient was a man who had a growth of about two years' duration behind the left ear. There was a history of its increasing and decreasing in size. When first seen, about three weeks previous to presentation, the mass was about the size of a small egg and apparently fluctuated. There was no rise in temperature and no pain. Roentgenographic examination showed a cholesteatoma of the right ear, but no bony cranial defect on the left side. An incision was made very carefully under synergistic anesthesia, and a growth, which seemed to be dural, was met. After opening the lower part, Dr. Pollock explored the inside with a finger and felt something like a tooth. On careful dissection the tumor came away without difficulty, and the wound healed by primary intention. Microscopic examination showed the growth to be a lipoma with calcareous degeneration.

Presentation of Specimen.—Dr. Pollock presented a specimen from a laryngectomy, and showed photographs illustrating the condition of the patient, a merchant, aged 67, who had begun to get hoarse about two years previously. He consulted his local physician, who treated him for six months without examining the larynx. He then consulted a specialist, who advised the use of radium and this had been used about a year previously. When the man consulted Dr. Pollock, the right side of the neck showed scarring from radium burns, but apparently the treatment had helped him, for his voice cleared up and no metastatic glands could be palpated. The same physician had advised more radium six months before, but the patient would not submit to further treatment. Examination revealed an irregular growth on the left side of the throat. Under suspension laryngoscopy, a piece of tissue was removed which proved microscopically to be squamous cell carcinoma. The patient was given the choice of three things: first, to let the condition alone; second, a tracheotomy; third, a laryngectomy. The latter was decided on. A two step operation was performed. About the middle of December a tracheotomy was performed, and about three days later the patient returned home, coming back on January 11 for the laryngectomy. He had had no trouble with the tracheotomy, but was kept under observation for three days before the laryngectomy was performed on January 14. It was necessary to change the entire method of operating. An incision was made which began at the angle of each jaw, and continued to a point below the tracheotomy opening, and a flap was raised which gave a good exposure. Dr. Pollock then started at the top and dissected off the larynx first. This offered great advantages. The patient was operated under synergistic anesthesia and was conscious all the time. Very little local anesthesia was used. In dissecting downward, Dr. Pollock dissected the mucous membrane as he went along, and had much more mucous membrane than usual. The second advantage of this method was that no blood ran down the trachea. The tracheotomy tube was kept in place until the larynx was entirely dissected; it was then removed, and a long rubber tube was used to plug the trachea up tight so that nothing could seep into the trachea from the wound. The opening was larger than usual, which was thought to be due to pressure from the tube that was placed in the trachea. The patient was making an excellent recovery and was up and about the hospital and grounds.

Some of the unpleasant things in laryngectomy are due to inhalation of material from the wound. In this case, the tube and packing were kept in place for eight days following the operation. The patient had been fed by an esophageal tube and had only a small pharyngeal fistula. On the right side,

where the large amount of radium had been applied, it was almost impossible to dissect the tissue out, while on the left side the dissection was easy. There had been no untoward result from the operation, and because of the method used there had been much more mucous membrane than usual to use in closing the esophagus.

PERITONSILLAR ABSCESS. REPORT OF CASE OF STREPTOCOCCUS INFECTION. Presented by DR. G. W. BOOT.

The patient was a well developed boy, aged 8, whom Dr. Boot had been called to see and to open a peritonsillar abscess on the right side. There was so much swelling that no anesthetic could be given. An incision was made with a blunt tonsil knife and extended through the mucous membrane and fascia only. No pus was obtained. The patient had previously had a discharge of pus from the nose; he also had an abscess in the left ear which Dr. Boot opened. The temperature was 105 F. The boy's condition improved steadily for about a week. The temperature returned to normal, the swelling disappeared from the peritonsillar region, but the left ear continued to discharge bloody pus. Dr. Boot was considering the advisability of a mastoidectomy, when one morning at 4:30 he was called by the nurse, who said the boy had had a severe hemorrhage, and probably lost two quarts of blood. He went to the patient immediately, but found the hemorrhage had ceased and there was nothing to show from whence it had come. The boy was given salt solution by enema and ceanothin by mouth. He was seen again at 8:30, and was semicomatose; he was ordered to the hospital for transfusion and a general surgeon gave 400 cc. of Ringer's solution under the breast and 100 cc. of the father's blood intramuscularly. Following this the boy's condition improved and he slept most of the day. At 2:45 p. m. he was in good condition, but within five minutes had another hemorrhage and died. Necropsy was not permitted, but by holding the mouth open and the palate up as well as possible with a blunt hook, Dr. Root could see an enormous vessel as large as a lead pencil running up behind the posterior pillar on the right. In the nasopharynx this vessel had sloughed through in two places, at least 1 inch above where the incision had been made for the peritonsillar abscess a week before. It was impossible to tell whether the vessel was an artery or a vein, but it appeared to be an artery. It lay just under the mucous membrane and just behind the posterior pillar.

DISCUSSION

DR. C. H. LONG thought it would not have been a bad plan if Dr. Boot had ligated the common carotid artery.

DR. J. HOLINGER recalled the patient he presented before the Society a number of years ago, in whom a large vertical pulsating blood vessel which was easily visible was parallel to one posterior pillar. Had there been a hemorrhage in that case there would have been no possibility of getting an aneurysm needle around it, or any way of getting to it. Since then, he had read reports of similar findings. Consequently, he thought such vessels occurred not infrequently and were very dangerous.

DR. SAMUEL SALINGER said that about a year ago at the meeting of the Royal Society of London, this question was discussed and it was the consensus that this vessel was a tortuous internal carotid artery which would remain so. The recommendation was to palpate this region of the pharynx preceding every tonsillectomy.

Dr. H. L. Pollock recalled a similar case which he had presented, in which he anesthetized the patient's throat and with a small stethoscope could hear the bruit in the vessel. The general belief was that this was an anomalous internal artery, and he believed all these cases were considered to be the internal carotid artery.

Dr. Boot (closing) stated that during life there was no apparent source of the hemorrhage, and no opportunity to ligate the internal carotid artery. He asked Dr. Pollock whether he had secured a section from the tumor in the case he presented, and if there was a possibility of its being a mixed parotid tumor.

Dr. Pollock (replying to Dr. Boot) said that they first suspected a dermoid cyst, for it felt as if it contained a tooth, but microscopic section showed it to be a pure lipoma with calcareous degeneration. The patient had a cholesteatoma in the opposite ear, but this had nothing to do with the ear which had the tumor.

Book Review

LEHRBUCH DER LOKALANASTHESIA DES OHRES UND DER OBEREN LUFT UND SPEISEWEGE. By DR. CAESAR HIRSCH, chief of the department of throat, nose and ear diseases of the Marien Hospital, Stuttgart, with an introduction by PROF. DR. FOSZ, director of the University Clinic, Frankfurt. Pp. 293, with 104 illustrations. Stuttgart: Ferdinand Enke, 1925.

This is a volume of 293 pages followed by twenty-three pages of references to literature and an index. The contents cover the entire subject of local anesthesia as applied to the head, neck, larynx and esophagus. The author goes into great detail about the various forms of local anesthesia, and the technic of superficial and injection anesthesia in the general part of the book. In the special part of the book, the author gives in detail the technic of local anesthesia in operations on the head, ears, eyes, nose, nasal sinuses, hypophysis, mouth and neck. The book is well illustrated. It undoubtedly represents the result of years of study and experience in this subject, and the feeling of the reviewer is that the book should fulfil a much needed place in medical literature. The descriptions of the technic for injection for local anesthesia are plain and definite, with a complete description of the various technics which are used.

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